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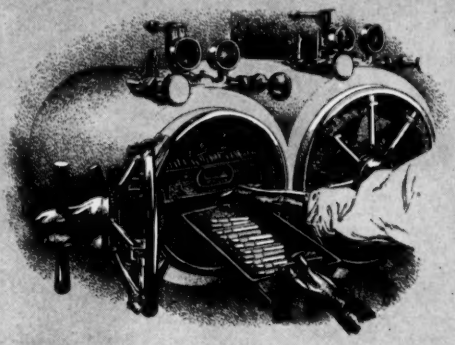

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VOLVULUS OF THE CECUM

With a Review of One Hundred Cases in the Literature and a Report of Six New Cases

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VOLVULUS of the cecum is regarded as a rare condition, but in many cases it has masqueraded for years as chronic or recurrent appendicitis before a severe attack revealed the true diagnosis. The number of cases in which the disease goes unmasked is unknown. When one considers the embryology of the intestinal tract and the many anomalies contained therein, it is surprising that volvulus of the cecum and of the terminal portion of the ileum does not occur more commonly. It is probable that many cases have existed, however, without having been reported.

The first description of cecal volvulus was written by Rokitansky in 1841. Since that time only from 300 to 400 cases have been reported. Most of the cases occurred in Central European countries and in Russia, where the incidence of cecal volvulus is greater than in England or in the United States. Jacobsen reported an incidence of acute intestinal obstruction due to cecal volvulus of 11.6 per cent; other European authors reported an incidence of about 5 per cent (Sweet). From 1916 through 1946 the "Quarterly Cumulative Index Medicus" listed sixty-three papers on torsion of the cecum, of which fourteen were published in the United States. In 1905 Corner and Sargent collected 57 cases and added 6 of their own. This report reviews the articles in the American and English literature and adds 6 cases which were observed in the Albany Hospital.

Acute intestinal obstruction occurs in the form of cecal torsion in the United States in about 1 per cent of cases. The following percentage incidence has been reported: at Massachusetts General Hospital, 1.15 per cent (Sweet); at Touro Infirmary, 1.4 per cent (Browne); at Harlem Hospital, 0.67 per cent (Rothman); at New York Hospital, 0.85 per cent (Cornell), and at Albany Hospital, 4.3 per cent.

Torsion or volvulus of the cecum has been defined as a "condition in which there is torsion, limited to the cecum, ascending colon and adjacent portion of the small intestine" (Grace, quoting Gastellier,

From the Department of Surgery, Albany Hospital and Medical College.

Moutier and Procher). The axis of torsion in cecal volvulus may be of three types, according to Weinstein: (1) the cecal bascule, in which the posterior surface of the cecum looks forward and the axis of rotation is transverse, (2) rotation in an oblique axis, in which the cecum may occupy the umbilical or even the left hypochondriac region and (3) rotation of the cecum about its long axis.

The cecum is the proximal portion of the large bowel that lies below the level of the top of the ileocecal valve. It is an asymmetric, thin-walled sac about 6 cm. in length by 7 cm. in width. In adults it usually lies in the right iliac fossa on top of the iliopsoas muscle, to which it is attached in varying degrees by areolar tissue. The ileum joins the cecum on its posteromedial aspect, and about 4 cm. below the appendix arises at the junction of the three tinia.

The cecum and the appendix first appear as an out-pocketing of the midgut about the sixth week of development. As the primitive intestine reenters the peritoneal cavity and starts to rotate around the axis formed by the superior mesenteric artery, the cecum and the appendix move to the left. About the eleventh or twelfth weeks they lie just below the liver to the left of the midline. From there they travel across to reach the right hypochondriac region about the fourth month. Uusually during the later months of intrauterine life and the first few months after delivery, the cecum descends into the right iliac fossa. While the descent is taking place, the great omentum grows down over the ascending colon and the cecum. The omentum and the ascending mesocolon then fuse with the primitive posterior parietal peritoneum. Anomalies of the cecum result if any of these processes stop short of completion or are carried too far. The various combinations that may occur are well described by Wolfer, Beaton and Ansen.

Hyperfixation of the hepatic flexure, ascending colon or terminal end of the ileum and hyperdescent of the cecum are contributing factors to torsion of the cecum, but the essential anomaly is hypofixation. Wangensteen has said that "volvulus of the cecum is only possible in the absence of fixation of the cecum or the presence of a mesocecum sufficiently mobile to permit torsion." Weinstein added that there must be a fixed point about which the bowel can rotate. Waugh laid stress on the ascending colon being the only segment of the intestine throughout the alimentary tract that has to support semisolid material against the action of gravity and to drive it vertically uphill. Elsewhere the contents are fluid or the path to be followed by them is oblique, horizontal or downhill. An abnormal mobility of the cecum and the ascending colon is a prerequisite to a volvulus of this portion of the intestinal tract, the degree of mobility depending on the length of the mesentery.

The structure of the cecum tends to aggravate torsion, once it has started. According to Alvarez' gradient theory of intestinal peristalsis,

the gradient of the cecum is low or reversed so that material tends to accumulate there. Cannon, working on the cat, showed that the receptively relaxed cecum and the ascending colon, on receiving the liquid contents of the small intestine, undergo activity in the form of antiperistalsis which retards and churns their contents for a considerable period. This delay favors both fermentation, with formation of gas, and absorption of fluid. In addition, the ileocecal valve is in many persons a competent one way valve so that liquid fecal material may continue to enter the cecum but material from the cecum cannot enter the ileum. Consequently, if there is an obstruction of lumen preventing the cecum from emptying, it distends rapidly, which embarrasses the blood supply and thereby reduces its absorptive power. As the cecum distends, it tends to kink across its long axis because the curve of the iliac fossa and the attachment of the ileum tend to pull it medially. Corner and Sargent emphasized the importance of acquired lateral pouches of the cecum, arising from the distending influence of gas produced by processes of bacterial fermentation in which stasis is present for some time. Flint spoke of the cecum as being a cesspool. According to Homan, there is a functional disturbance in which a "most interesting but little understood factor is the power of rapid gas formation possessed by the intestinal tract." Weinstein theorized that the rapid distention in the involved loop is due to deficient oxygen supply to the twisted loop, which favors the growth of anaerobic bacilli.

Various authors have measured the mobility of the cecum at the time of necropsy. Harvey found unnatural free motion of the cecum and the ascending colon in 13.3 per cent of examinations performed on 105 infants at necropsy; Piersol found it in 14 per cent, Treves in 26 per cent and Smith in 31 per cent. According to Grace, it has been estimated that from 10 to 19 per cent of cadavers "show a degree of mobile cecum sufficient to permit volvulus to develop, there being a congenital lack of adequate fixation of the cecocolon." Chalfant reported that there was excessive mobility of the cecocolon in about 20 per cent of persons of all ages, and Wolfer and others found that in 11.2 per cent the "cecum was sufficiently mobile as to allow the development of a volvulus" (in 125 normal cadavers). Torsion of 180 to 360 degrees is common, but it may occur up to 520 to 720 degrees. Tightness of the twist rather than the number of turns determines whether the pathologic changes of necrosis will follow. The direction of the twist is usually clockwise but may be counterclockwise.

There are, however, precipitating causes which must be considered in conjunction with altered anatomy and physiology. Pratt and Fallis stressed the belief, from their research on the subject, that extremes in diet and physical exertion should be seriously considered when there is an abnormal development of the intestinal tract. The higher pro-

portion of cases in Finland and Russia, where the diet consists mostly of potatoes and bread, helps to substantiate the theory that undigested, coarse, vegetable fibers act as an irritant to the colon, which is essentially a cesspool, and that as a result abnormal peristalsis is produced.

Cabot remarked that "for some unknown reason, twists occur much more frequently in those cases whose peritoneum has been damaged by a previous operation or inflammation, even when no constricting bands of adhesions can be found." This premise is substantiated by the many cases reviewed by us. Many other exciting causes have been mentioned by various contributors to the literature on this subject, i. e., old scar formations, bands, chronic mesenteric adenitis, former operations, hernias, foreign bodies, mesenteric cysts, fecaliths, chronic intestinal stasis, tumors and pregnancy. Eustis mentioned typhoid fever as being a predisposing factor. Wangensteen stated that volvulus concomitant with carcinomatous obstruction at the flexure does occur.

Roentgenology can be an aid in the diagnosis of this condition but usually only as an adjunct to the various clinical findings. The interpretation of intestinal obstruction is easily made, but to isolate certain segments of the intestinal tract is a different matter. It is well accepted by roentgenologists that if upright or lateral roentgenograms are made fluid levels can usually be seen in almost any type of real ileus but especially in obstruction of the colon. In most cases obstruction of the colon is of the closed loop type, that is, the ileocecal valve remains "competent" and hence there is little or no distention of the small intestine. Furthermore, if only a portion of the colon is distended by gas and a point can be found beyond which the column of gas is absent or greatly diminished, it is highly significant. Sailer pointed out that the cecum appears to be a region of particular accumulation and that there is a somewhat clearer area in the hepatic flexure on retention of bismuth in the cecum for more than twenty-four hours.

Easton described a "new sign" which he explained as follows:

> During the course of a barium enema, the column of barium is unable to pass beyond a certain point in the region distal to the cecum, i. e., in the ascending or transverse colon (organic lesions excluded) so that the cecum cannot be properly delineated in its marking by the barium, and when, at the same time, a large collection of gas appears at the site of the cecum, indicating its patency and conformation, either in the midline or slightly to the right of it, this is a clear sign that volvulus of the cecum had taken place.

Rothman suggested the following procedure: Take a roentgenogram on entry of the patient to the hospital and start Wangensteen drainage and enema. Take another roentgenogram and compare; the gas bubble will be in the same position and will have the same configuration. It may possibly be slightly larger, which means a closed loop obstruction;

the size and the fluid level indicate involvement of the colon. From the position, one may diagnose volvulus of the cecum, as sigmoidal volvulus presents a different picture.

The signs and symptoms of a volvulus of the cecum are as a rule bizarre. From observation of our own cases and from the data obtained from a review of the cases which have been analyzed, there is no definite sign or symptom complex. On the other hand, the patient's history and the presence of localized tympany, distention or mass may be of the greatest aid in forming a preoperative diagnosis.

Marnoch laid stress on local tympany and distention. From a study of reported cases he concluded that the less the small intestine is involved the more prominent is this symptom in obstruction of the large bowel. Treves spoke of the irregularity of distention and Wangensteen of the acuteness in volvulus of the cecum or small intestines as compared with torsion of the pelvic colon. According to our observations and those of others, the early absence of abdominal clicks is of importance.

Ingelfinger stated that of 81 patients studied 47 per cent exhibited chronic symptoms before the acute onset. Small stated that in a series of 190 patients with mobile cecum 79 had previously undergone operation for "chronic appendicitis." Chalfant advised that "the diagnosis of torsion of the cecum should be thought of with patients presenting a history of obstinate constipation with previous attacks of severe pain in the upper abdomen." Sweet made the statement that "clinically there are signs of intestinal obstruction with perhaps localized abdominal distention in the right half of the abdomen or the presence of a large tympanitic mass, in this region, suggesting a dilated cecum." Coughlin quoted Coffee, who said: "I am convinced that over one-half of the patients complaining of right sided pain have no definite organic disease but have defective fixation of the ascending colon and that x-ray so often shows a fairly movable cecum and ascending colon." Evans and Bigger, in their recent communication, mentioned the sign of "position of relief," i. e., any position in which the patient is free of his pain, as highly suggestive of obstruction of the bowel.

The abdomen may be silent early; if sounds are present, they are generally of a low pitch. Early shock is infrequent. At times rectal or vaginal examination helps to confirm the diagnosis. Gaseous distention often produces an early and typical tender tympanitic swelling, usually in the right lower quadrant. Before volvulus becomes permanent, it may cause colicky pain in the ileocecal region for one or two days. There are the usual signs of intestinal obstruction, with considerable inflation of this part of the bowel.

In reviewing the data on 100 cases (including 6 of our own), we have attempted to make an analysis based on the following observations.

SUMMARY OF ONE HUNDRED CASES

Age.—The highest incidence occurs in the 25 to 30 age group, with the 20 to 25 age group second, although the average age of the patients is 39.8 years. The appended chart shows the age distribution.

Sex.—From a review of the literature it is apparent that there is little difference in the sex factor. There were 50 men and 50 women.

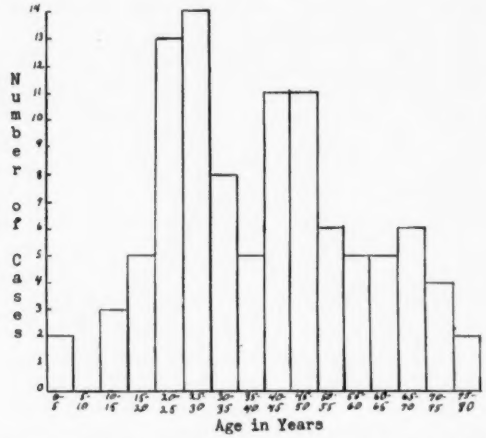

Fig. 1.—Age distribution among 100 patients with volvulus of the cecum.

TABLE 1.—*Operations Performed Before Onset of Intestinal Obstruction*

No.	Type of Operations	Elapsed Time
3.	Herniorrhaphy (right inguinal area)	72 hr., 4 yr., 16 mo.
2.	Umbilical herniorrhaphy	4 yr., "years ago"
1.	Umbilical herniorrhaphy and cholecystectomy	"Years ago"
5.	Appendectomy	7 days, 5 yr., 6 yr., 18 yr. and "years ago"
1.	Appendectomy and gastroenterostomy	9 days
1.	Drainage of appendical abscess	4 yr.
2.	Cholecystectomy	4 days, 4 yr.
1.	Removal of renal calculus	7 yr.
1.	Volvulus of sigmoid (detorsion)	2 previous detorsions, "years ago"
1.	Cecopexy	5 mo.
2.	"Many abdominal operations"	"Years ago"
1.	Gastroenterostomy	4 days

Previous History.—Seventy-three patients gave a history of positive symptoms, varying from mild to severe indigestion, or of attacks which were similar but of less severity than the one which caused their admission to the hospital. Practically all in this group complained of constipation. In 19 cases the history was noncontributory, and in 8 the previous history was not mentioned.

Previous Operations.—Operations had been performed before the acute onset of intestinal obstruction in 21 per cent of cases. The types are listed in table 1. The lapses of time between operation and torsion of the cecum were as follows:

Under 10 days	5, or 23.8%
Between 1 month and 2 years	2, or 9.5%
Between 2 years and 5 years	4, or 19.0%
Between 5 years and 10 years	2, or 9.5%
Between 10 years and 20 years	2, or 9.5%
"Years ago"	6, or 28.5%

Pregnancy.—In 10 cases the obstruction accompanied pregnancy.

Distention, Nausea and Vomiting.—Practically all patients who gave a complete history had these symptoms.

Rigidity.—Fifteen had rigidity and 11 had no rigidity; in 74 cases rigidity was not mentioned.

Visible Peristalsis.—Visible peristalsis was present in 7 and absent in 13; in 80 cases there was no mention of peristalsis.

TABLE 2.—*Types of Operation Performed on Patients With Gangrenous Cecum*

No.	Type of Operation	Recovery	Death
10.	Resection	4	6
8.	Detorsion and cecostomy	3	5
1.	Ileostomy	..	1
1.	Died on table	..	1
5.	No operation	..	5
	Total	7	18
	Mortality (for those operated on) 65%		
	Mortality (no operation) 100%		

Intestinal Clicks.—Intestinal clicks were present in 16 and absent in 5; in 79 cases no mention of this symptom was made.

Masses.—Masses were present in 29 cases.

Pain.—All patients complained of abdominal pain, but in 51 cases no definite presenting localization was noted. In the remaining 49 cases, the localization was as follows: The epigastrium was involved in 2 cases, the right upper abdominal quadrant in 10, the right lower abdominal quadrant in 17, the periumbilical region in 5, the suprapubic region in 4 and the left lower abdominal quadrant in 2. The pain was diffuse in 9 cases. In 51 cases the pain was reported as colicky at first, and in 5 it was reported as steady at first. In the great majority of cases pain became diffuse within a few hours.

Shock.—Twenty-four patients experienced shock.

Duration of Symptoms.—The duration varied from a few hours to a few days, although many records were so indefinite that a true evaluation could not be made.

Gangrene.—Twenty-five patients presented a gangrenous cecum either at operation or at necropsy. Of these, over 75 per cent came

for treatment before the fifth day. Most of those who survived, however, were operated on within twenty-four hours of the onset of acute symptoms. The data are given in table 2.

The results of operation on patients with and without gangrene are given in table 3.

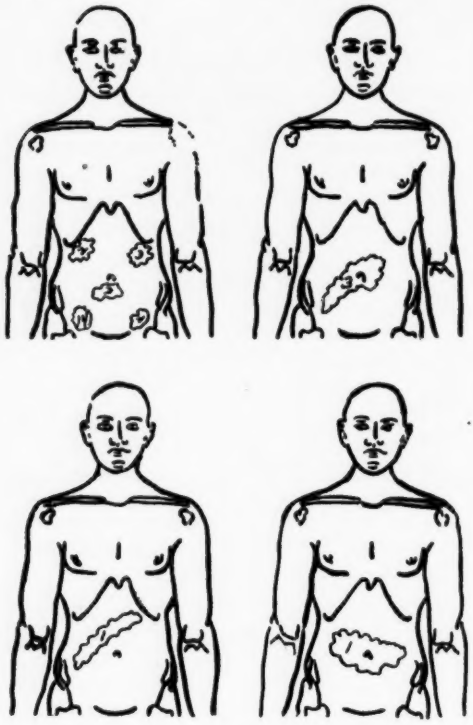

Fig. 2.—Location of masses.

Eighty-three patients were operated on. The type of treatment given to the other 17 patients was not mentioned, but of these, 7 were reported to have died and 3 recovered.

	Number	Recovered	Died
Operated on	83	50	33
No operation (excluding those with gangrene)	2	..	2
Treatment and result not recorded	5	?	?
Treatment not recorded	10	3	7
Total	100	53	42

REPORT OF CASES

CASE 1.—J. E. P. (service of J. L. Donhauser), a 73 year old white man, entered the hospital with the presenting symptom complex of severe persistent pain in the lower part of the abdomen, vomiting and constipation of approximately eighteen hours' duration. For the past four days the patient had not felt well because of difficulty in moving his bowels and some difficulty in passing urine. Approximately eight hours before his admission the abdominal pain increased in severity and became constant in the lower right quadrant, and within a few hours he vomited copious dark green foul-smelling material. During the ensuing few hours he passed a small watery stool containing bright red blood. This alarmed him considerably, and he sought medical aid. About twenty years previously an appendical abscess had been drained, and ten years subsequently a cholecystectomy had been performed.

Physical examination showed a well developed, obese man in partial shock; his respirations were rapid, shallow and grunting, and he was extremely apprehensive. His face was pallid, the lips were cyanotic, the lower extremities were mottled and of a dusky hue and the skin was clammy and cold. The abdomen

TABLE 3.—*Operative Results*

	Recovered	Died
Aspiration	1	0
Cecostomy	21	13
Cecopexy	10	2
Detorsion (alone)	12	2
Enterostomy	0	1
Exteriorization	1	3
Exploratory laparotomy	0	1
Mikulicz' operation	2	0
Resection	3	11
Total	50, or 60.2%	33, or 39.7%

was full and obese, somewhat distended and slightly irregular. There were no intestinal patterns or waves noted; there was considerable spasm of the entire abdominal wall, but exquisite tenderness and spasm were found in the right lower quadrant. No masses were present and no intestinal clicks audible.

The roentgenographic appearance of the abdomen is given in figure 3.

The patient was operated on under "pentothal sodium" anesthesia within two and one-half hours from the time of his admission to the hospital. A right rectus incision was made. The cecum was found to be huge, about the size of a medicine ball, embedded in diffuse pericecal adhesions and completely gangrenous. It had completely twisted on itself in clockwise fashion. While the volvulus was being untwisted and an attempt made to deliver it, the cecum was ruptured and fecal material covered the operative field. The cecum was deflated, and after a tube was inserted it was exteriorized. Death ensued the following morning. It was interesting to note that at necropsy carcinoma of the hepatic duct and prostate gland was found. There was apparently no relation between the carcinoma and the cecal torsion.

CASE 2.—E. H., an elderly man (service of J. L. Donhauser), entered the hospital because of abdominal discomfort, distention and complete obstipation for seven days. He stated that nine days before he had had colicky pains, especially severe in the right abdominal quadrant, and of a lesser degree in the right lower quadrant. This

pain persisted for two days, after which it became lessened, and it completely subsided after six days. Repeated enemas had been ineffectual, with the exception of the passing of a "little gas." He was nauseated once but did not vomit. The patient's history was noncontributory so far as previous attacks were concerned, but he admitted that years ago he had had "an inflammation of the gallbladder." The bowels had been regular up to two weeks before his admission.

Physical examination showed an extremely thin man who spoke with a hoarse voice and was in apparent distress (discomfort due to abdominal distention). The temperature was 98.6 F., the pulse rate 84, the respirations 24 and the blood

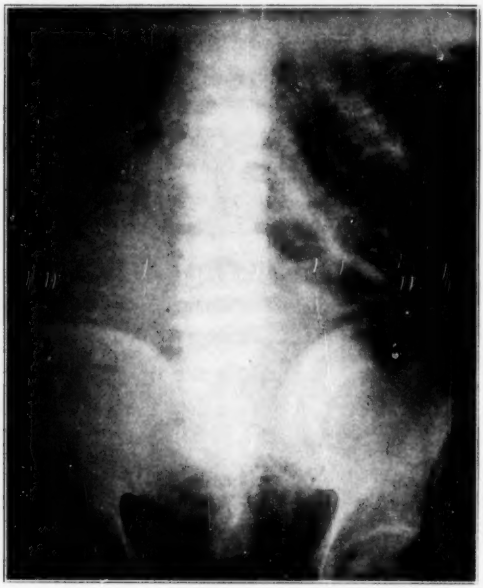

Fig. 3 (case 1).—There are several distended loops of the small bowel to the left of the midline, suggesting intestinal obstruction. A large amount of retained material was visible in the cecum.

pressure 142 systolic and 90 diastolic. The abdomen was much distended and markedly tympanitic throughout. Hepatic dulness was completely absent. The abdomen was symmetric; no peristalsis was noted and no mounds felt. A few indistinct "clicks" were heard scattered over the abdomen. A slight shifting dulness was detected, although there was no definite dulness over the flank. Palpation revealed nothing abnormal with the exception of slight tenderness in the left flank. There was no rigidity.

The roentgenographic appearance is shown in figure 4.

Operative Findings.—When the peritoneum was opened, a small amount of free fluid was encountered. No gas or pus was noted, but there was a tremendous dilatation of the cecum, ascending colon and small intestine. The distal portions

of the transverse colon and descending colon were not dilated. The small bowel was found to be wrapped around the sigmoid and the colon, which were on a long redundant mesentery. However, this did not explain the obstruction. A hard band was found running from the ascending colon to the lateral parietal peritoneum which appeared to be holding up the cecum. This was severed. The cecum was delivered into the wound and found to be dilated to a diameter of about 6 to 8 inches (15 to 20 cm.). Both it and the ascending colon were on a long mesentery and had twisted once on themeslves (clockwise). Detorsion was carried out, with recovery.

CASE 3.—Fifteen years before his admission to the hospital J. C. (service of J. L. Donhauser) was operated on for the repair of a hernia in the right inguinal area. Two years later, after an accident, there was a recurrence. A second herniorrhaphy was performed in the usual manner, with a transplantation of the cord. Postoperatively, the patient had considerable distress from persistent abdominal distention, nausea

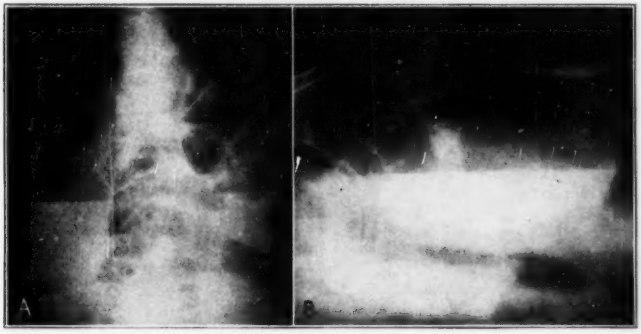

Fig. 4 (case 2).—*A*, a flat plate roentgenogram of the abdomen shows enormous dilatation of the loops of the small intestine, consistent with obstruction of the small bowel. There is a large accumulation of air in the peritoneal cavity over the dome of the liver on the right side, and there are multiple fluid levels in the small intestine and in the peritoneal cavity. *B*, The findings are consistent with obstruction of the small bowel, with a probable perforation of the viscus, and the free air in the peritoneal cavity may be the result of gas-forming organisms.

and vomiting. This lasted for one week. He gradually improved, though a soft distention stilled persisted. He complained of abdominal pressure and of considerable gas, but he was able to walk around on the eighteenth day. During this siege, flouroscopy and a flat plate roentgenogram revealed the presence of "pneumoperitoneum." No etiologic factor could be found to account for this condition, and at that time surgical intervention was not apparently indicated.

One year later the patient was admitted to the hospital because of abdominal pain, nausea and vomiting. The presenting symptom at this time was sharp epigastric pain. From his story, it would appear that he had felt perfectly well until two weeks before his admission, during which time he had "indigestion and stomachache." Two days before his admission sharp epigastric pain with diffuse abdominal radiation occurred and there were several episodes of nausea and vomiting. There had been no evacuation of stools for thirty-six hours. A slight bowel movement was obtained by means of an enema.

Physical examination revealed a fairly well nourished man, 53 years of age, in moderate distress. He looked extremely sick. There was general arteriosclerosis present (Wassermann reaction positive), and on inspection of the abdomen, there was noted a large sausage-shaped area of distention running diagonally across the abdomen from the left upper quadrant to the right lower quadrant and being from 15 to 20 cm. in length. The mass was tense, tender and tympanitic, and there were tenderness and moderate spasm in the right lower quadrant. In the epigastrium slight tenderness was noted. The abdomen was tympanitic throughout. There was no visible peristalsis. On auscultation, intestinal clicks were increased, but no "rushes" were audible. The temperature, pulse and respirations were within normal limits. The blood pressure was 155 systolic and 95 diastolic. The white blood cell count was 92,000. The urine was essentially normal. The blood sugar content was 424 mg. per hundred cubic centimeters, the nonprotein nitrogen 55.4 mg., creatinine 2.1 mg. and chlorides 270 mg.

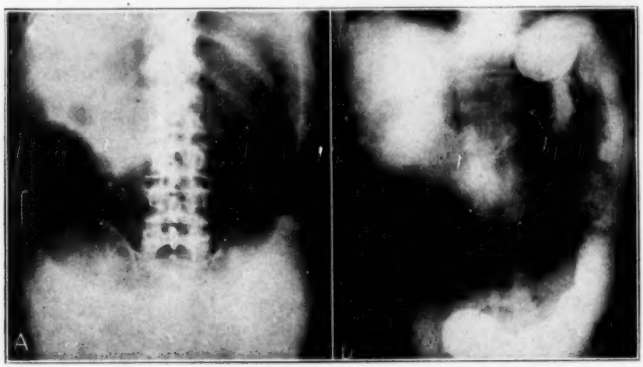

Fig. 5 (case 3).—*A*, a preliminary roentgenogram showed large accumulation of gas which suggested the stomach in outline. Barium administered by mouth filled the upper portion of the stomach; the latter structure was normal in size and appeared to lie below the gas-containing shadow. There was evidence of a fluid level in the large saclike accumulation of gas, visible when the patient was brought to a vertical position. *B*, a barium enema filled the large intestines up to the splenic flexure, and some of the barium passed into the transverse colon. There was no alteration of the gas pattern described except that it appeared to be smaller in an anteroposterior posture.

The roentgenographic appearances are shown in figures 5 and 6.

The patient was operated on seven and one-half hours after his admission to the hospital. When incision into the peritoneal cavity was made, a large amount of pink-gray fluid escaped. This was evacuated, and it was then noted that a greatly distended deep purple-colored segment of intestine bulged forth and occupied the entire incision. The diameter of this portion of intestine was approximately 15 cm. After slight manipulation, the intestine burst, and fecal material oozed forth. Traction on the cecum revealed it to be completely rotated on itself three times. The ileum to which it was attached had undergone a complete turn. The cecum was untwisted and found to be completely gangrenous. Cecostomy was performed. The patient died from general peritonitis.

CASE 4.—L. T. (service of A. Wallingford), a 38 year old white married woman, was admitted to the hospital because of severe colicky pain in the right upper abdominal quadrant, with vomiting. The patient stated that she had been perfectly well until the evening before her admission. There had been no history of previous attacks. Twelve years ago she had had her appendix removed. The bowel movements had been regular. She was eight months pregnant.

Examination of the abdomen showed an enlargement consistent with an eight months pregnancy. Another enlargement to the right and superior to the uterine fundus (evidently ballooned intestines) was observed. Maximum tenderness with-

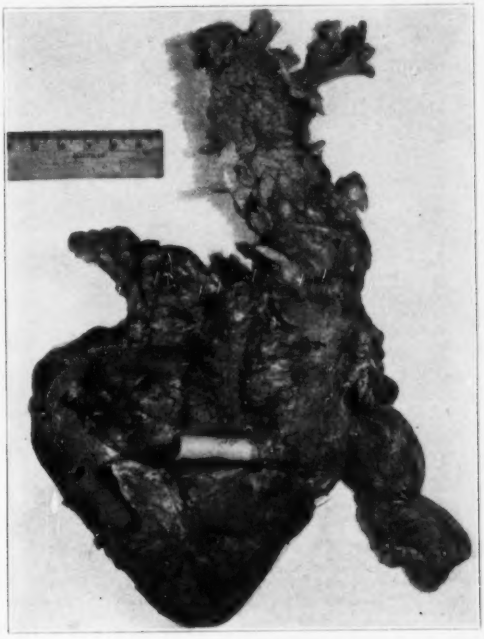

Fig. 6 (case 3).—Gangrene of cecum, ileum and mesentery due to torsion facilitated by abnormally mobile ileum and cecum.

out rigidity was noted over the right upper quadrant (upper end of an old scar from an appendical operation). On stethoscopic examination, a clear bell-like tinkle or "peristaltic jingle," suggesting obstruction of a loop of intestine, with jostling of fluid inside, was heard.

The roentgenographic appearance is shown in figure 7.

The patient was operated on nine and one-half hours after her admission to the hospital. At operation, loops of the terminal end of the ileum presented themselves greatly distended with gas. The cecum had made a complete revolution. There were adhesions from the cecum to the upper fold of a loop of the terminal

end of the ileum about 2 feet (61 cm.) from the ileocecal valve. The cecum was extremely mobile after its release. Detorsion cured the condition, and the patient made an uneventful recovery.

CASE 5.—D. B. (service of A. W. Elting), a 23 year old white mechanic, was admitted to the medical service and transferred to the surgical service about one week after the onset of abdominal pain, fever, lethargy and anorexia. The diagnosis, as verified by the laboratory, was typhoid fever. The patient was apparently making an uneventful recovery until the tenth day after his admission, when he awakened early in the morning complaining of abdominal pain. The pulse rate, which had been consistently between 90 and 100, had risen to 130; it then fell to 70. The abdomen became distended and diffusely tender; no spasm could be elicited except

Fig. 7 (case 4).—A flat plate roentgenogram of the abdomen showed considerable distention of the ascending colon and of a portion of the transverse colon. A fetus is visible within the abdomen, in breech presentation.

in the right lower quadrant. It was felt that the patient was suffering from a perforation of the bowel or from hemorrhage.

Examination revealed the following symptoms: The abdomen was somewhat distended and asymmetric, with increased prominence in the lower right abdominal quadrant, particularly marked toward the midline. The costal and iliac grooves were obliterated. Respiratory movements were present in the upper part of the abdomen and practically absent in the lower part. There were no visible patterns. On palpation, there was a definite resistance of the upper abdominal wall, which did not appear to be tender. In the lower part of the abdomen, particularly in the right lower quadrant, resistance was increased and discomfort was pronounced. There was the sensation of a mass behind the abdominal wall occupying the lower median portion of the right quadrant of the abdomen and corresponding to the

asymmetric prominence. This area as well as the rest of the abdomen was tympanitic. Rectal examination showed some accumulation pressing into the pelvis from the right side, which was interpreted as an early peritoneal accumulation or as dilated intestine. The white blood cell count was 5,300.

With the patient under anesthesia produced by gas, oxygen and procaine hydrochloride infiltration, an exploratory laparotomy was performed. A tremendous volvulus of the cecum was found (fig. 8). The bowel was so dis-

Fig. 8 (case 5).—Volvulus of cecum complicating typhoid fever. The anterior wall of the cecum has turned to the right 180 degrees and has carried the terminal ileum with it. The terminal end of the ileum can be seen lying anteriorly and entering it on what is now its right side.

tended that it was impossible to manipulate it, so that after a decompression a cecostomy was performed and the patient returned to his room in fairly good condition. Five days after operation the pulse became of poor quality and the abdomen moderately distended and a bilateral cervical adenitis developed. Within a few hours distinct glossitis developed. The temperature rose to 104 F. A blood culture was taken, which was subsequently reported as showing the presence of hemolytic streptococci. On the sixth day after operation the patient died.

CASE 6.—Mrs. M. L. (service of A. Wallingford) was admitted to the hospital with the chief complaint of pain in the right side of her abdomen, approximately 3 cm. to the right of the umbilicus. The patient stated that she had been perfectly well until six hours before her admission, when pain developed in the abdomen; four hours later she became nauseated, and on her admission to the hospital she vomited. There was no radiation of pain, and she had had a bowel movement eight to ten hours previous to the onset.

Physical examination showed a well developed woman, 43 years of age, in acute distress and complaining of nausea and of abdominal pain. The abdomen was tender and tense just to the right of the umbilicus. No mass could be felt, and there was no visible peristalsis. Peristaltic clicks were accentuated, and borborygmi could be heard. The urine was normal. The white blood cell count was 13,600. The temperature was 99 F., the pulse rate 90 and the respirations 22.

The patient was operated on ten and one-half hours after her admission to the hospital. At operation, a large mass the size of a football was found to be the cecum. After delivery of the cecum, it was seen to be obstructed at a point approximately 20 cm. from its tip and just beneath the hepatic flexure; the cecum had been twisted on itself three times, rotating from right to left. The torsion was untwisted and the appendix removed. Roentgenograms had not been taken. The patient recovered.

An analysis of the signs and symptoms ascertained in this series of 6 cases shows the following:

1. Pain was of a colicky nature in 3 cases and constant in 3 cases, and it was most commonly found, in the beginning at least, in the right upper abdominal quadrant or in the epigastrium.

2. Nausea and vomiting were present in all but 1 case, and in this case extreme nausea was present but no vomiting.

3. In all but 1 case enemas were effectual. This strengthens the idea that fairly good results with enemas may be obtained even though there is an obstruction (low in the bowel).

4. Distention, either symmetric or asymmetric, is a practically constant finding.

5. Abdominal rigidity is not a prominent feature unless gangrene, with or without perforation, has occurred, and abdominal tenderness, generally at least, is over the area of torsion.

6. Roentgenologic evidence is not conclusive, but a careful study of the roentgenograms, if the possibility of torsion is borne in mind, might well lead to a more perfect preoperative diagnosis.

7. Visible peristalsis is not as commonly found as in volvulus of the sigmoid, and in our series this sign was absent in all cases.

8. Operative procedure should be immediate, and the patient should be treated according to the condition found.

9. Shock is present in cases in which gangrene has occurred.

10. Cecal torsion should be considered as a diagnosis when the presenting signs and symptoms are found in the two right abdominal quadrants and when there are roentgenologic signs of cecal distention.

11. A preoperative diagnosis, other than one of intestinal obstruction, may be impossible.

12. The possibility of cecal volvulus should be borne in mind before a diagnosis of acute appendicitis is made.

13. A previous history of indigestion, constipation and mild attacks similar to those present on the patient's admission to the hospital is commonly noted.

SUMMARY BASED ON ONE HUNDRED CASES

Torsion of the cecum may occur at any age, but in 50 per cent of the cases it occurs in patients between the ages of 20 and 45.

It occurs in men and women in equal ratio.

Most patients give a history of previous attacks.

The signs and symptoms usually are those of obstruction of the bowel. Considerable distention and a mass are often present.

Pregnancy, previous operation, high roughage diet, strong catharsis, dietary indiscretions and unusual exertion are some of the predisposing or precipitating factors.

CONCLUSIONS

1. For torsion to occur, there must be hypermobility of the cecum, which is present in 20 per cent of the population, and a fixed point about which the cecum may rotate.

2. Torsion of the cecum, particularly partial torsion, is more frequent than the reported incidence would suggest.

3. It should be considered in cases in which there is pain in the right side together with a long history of constipation and of previous attacks of abdominal pain.

4. If the roentgenogram of the abdomen shows the pattern of obstruction of the small bowel and there is a markedly dilated loop of bowel on the right side, a diagnosis of torsion of the cecum should be considered. If the roentgenogram made after a barium enema shows the column of barium stopping in the hepatic flexure or in the ascending colon, it is further evidence of the existence of this condition.

5. The type of operation performed depends on the conditions encountered and has little effect on the mortality figures, but the earlier the operation, the better the results.

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SITUS INVERSUS WITH ASSOCIATED ABNORMALITIES

Review of the Literature and Report of Three Cases

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SITUS inversus, less commonly called transposition of viscera or heterotaxia, has been known from ancient times. Aristotle[1] cited 2 cases of transposed organs in animals. Fabricius,[2] in 1600 A.D., described a case of transposed liver and spleen in a human being. In 1824, Kuchenmeister,[1] first diagnosed situs inversus in a living human being and Vehsemeyer,[3] in 1897, demonstrated the condition by roentgen rays. In a review of the literature in 1926, Cleveland[4] collected 400 cases up to the end of 1924. Larson,[5] in 1938, estimated there had been 75 additional cases reported up to that time.

In reviewing the literature from 1925 to 1946, inclusive, I found 632 cases of situs inversus, of which there were 515 examples of dextrocardia, 379 instances of situs inversus totalis, 128 persons in whom dextrocardia was known to be the only form of transposition, 41 cases of partial situs inversus, 46 cases involving only the colon, 20 cases involving only the great vessels of the heart, 6 cases involving the stomach alone and 2 cases involving the liver alone. Among the 515 instances of dextrocardia there were undoubtedly a large number of situs inversus partialis or totalis—yet the information given by the various authors was so meager, or the author had so little interest beyond the heart, that no other diagnosis than dextrocardia could be arrived at. Cleveland and I together have collected 1,032 cases from the literature. Since it is undoubtedly true that many other examples of transposition of the viscera are encountered which are not reported,

1. Wood, G. W., and Blalock, A.: Situs Inversus Totalis and Disease of Biliary Tract: Survey of Literature and Report of Case, Arch. Surg. **40**:885 (May) 1940.

2. Lineback, P. E.: An Extraordinary Case of Situs Inversus Totalis, J. A. M. A. **75**:1775 (Dec. 25) 1920.

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4. Cleveland, M.: Situs Inversus Viscerum: Anatomic Study, Arch. Surg. **13**:342 (Sept.) 1926.

5. Larson, C. P.: Situs Inversus with Other Congenital Anomalies, Canad. M. A. J. **39**:474, 1938.

the condition must be much more frequent than has been generally supposed.

The frequency of occurrence varies greatly with different authors. Sherk [6] found situs inversus ten times in 347,000 admissions to the Mayo Clinic in the twelve year period 1910-1922. Willis,[7] in 1925, found 3 cases in 10,000 admissions to the same institution. LeWald [8] found 29 examples in 40,000 roentgenologic studies and 1 in 35,000 physical examinations in the United States Army. Rösler [9] found 3 cases in 22,402 autopsies. Adams and Churchill [10] found 23 instances in 232,112 admissions to the Massachusetts General Hospital. Balfour [11] found 51 cases in the Mayo Clinic in a twenty-one year period, 1918 to 1939. Parson [12] found 2 patients with dextrocardia, an anomaly frequently associated with situs inversus totalis, in 15,000 private patients. Cleveland found 1 case in the anatomic laboratory of the Columbia University College of Physicians and Surgeons during a period of forty years, during which about 10,000 subjects had been examined in routine dissection. Thus, the incidence given by different authors varies from 1 in 35,000 to 1 in 1,379. It is apparent that there is a great variability in the frequency of recognition, and possibly of occurrence, of this condition. The figure 1 in 7,467 given by Rösler, as found in 22,402 autopsies, might possibly be accepted as the nearest possible approach to the correct incidence of this condition, with the recognition that autopsies, being performed almost exclusively on hospital personnel, comprise a further selectivity as compared with the general population.

Situs inversus has many variations. While dextrocardia may occur alone, it is most frequently associated with situs inversus.[13] Many other congenital and acquired lesions of the heart are frequently seen, such as angina pectoris,[14] chronic rheumatic aortic and mitral endo-

6. Sherk, H. H.: Total Transposition of Viscera, Surg., Gynec. & Obst. **35**:53, 1922.

7. Willis, B. C.: Appendicitis and Transposition of Viscera, Ann. Surg. **82**:256 (Aug.) 1925.

8. LeWald, L. T.: Complete Transposition of Viscera, J. A. M. A. **84**:261 (Jan. 24) 1925.

9. Rösler, H.: Beiträge zur Lehre von den angeborenen Herzfehlern, über die angeborene isolierte Rechtslager der Herzens, Wien. Arch. f. inn. Med. **19**: 505, 1930.

10. Adams, R., and Churchill, E. O.: Situs Inversus, Sinusitis, Bronchiectasis, J. Thoracic Surg. **7**:206, 1937.

11. Balfour, D. C., cited by Wood and Blalock.[1]

12. Parson, G. W.: Dextrocardia with Situs Inversus Complicated by Chronic Rheumatic Aortic and Mitral Endocarditis, Ann. Int. Med. **23**:102 (July) 1945.

13. Capone, A. J., and Miller, H.: Left-Sided Appendicitis in a Dextrocardiac Patient, Am. J. Surg. **71**:282 (Feb.) 1946.

14. Cain, J. C.: Angina Pectoris Associated with Dextrocardia and Situs Inversus, Am. Heart J. **30**:202 (Aug.) 1945.

carditis,[15] myocardial infarction,[16] calcareous aortic stenosis and cor bovinum,[17] cor biloculare,[18] persistent truncus (ductus) arteriosus, abnormal systemic and pulmonic veins,[19] arrested cardiac development,[20] diverticulum of the heart,[21] cor triloculare biventriculare,[22] transposition of the large vessels of the heart,[23] aortic aneurysm,[24] aneurysm of the auriculoventricular septum [25] and Roger's disease (congenital defect in interventricular septum).[26] The respiratory tract may show such anomalies as transposition of the lungs—three lobes being situated on the left and two on the right [4]—congenital absence of one lung,[27] bronchiectasis and absence of or defective development of the paranasal

15. Silberstein, A. G., and Steinberg, I.: Contrast Cardiovascular Study of Patient with Rheumatic Mitral Valvular Disease and Dextrocardia with Complete Situs Inversus, New York State J. Med. **43**:1755 (Sept. 15) 1943.

16. Geeslin, L. E., and Tyler, G. R.: Myocardial Infarction in Congenital Dextrocardia, South. M. J. **37**:428 (Aug.) 1944.

17. Pasternack, J. G.: Complete Situs Inversus: Case with Calcareous Aortic Stenosis and Cor Bovinum, New England J. Med. **227**:953 (Dec. 17) 1942.

18. Walls, E. W.: Unusual Case of Congenital Cardiac Abnormality with Partial Situs Inversus, Anat. Rec. **82**:497 (April 25) 1942. Rossman, J. J.: Cor Biloculare with Transposition of the Great Cardiac Vessels and Atresia of the Pulmonary Artery: Phylogenetic and Ontogenetic Interpretation, Am. J. Clin. Path. **12**:534 (Oct.) 1942.

19. Goltman, D. W., and Stern, N. S.: Case of Dextroposition, Persistence of Early Stage of Embryonic Development of Heart, Persistent Truncus Arteriosus, Abnormal Systemic and Pulmonic Veins, and Subdiaphragmatic Situs Inversus, Am. Heart J. **18**:176 (Aug.) 1939.

20. Garrison, R. E.: Case of Situs Inversus with Asymptomatic, Arrested Cardiac Development, Wisconsin M. J. **38**:882 (Oct.) 1939.

21. Dietlen, H.: Case of Transposition of Viscera with Diverticulum of Heart, Ztschr. f. Kreislaufforsch. **20**:225 (April 15) 1928.

22. Smith, J.: Unusual Malformation: Cor Triloculare Biventriculare with Mirror Picture Dextrocardia, Brit. J. Child. Dis. **27**:26 (Jan.-March) 1930.

23. Dagnini, G., and Gelli, G.: Transposition of Large Blood Vessels of Heart, Clin. pediat. **13**:1 (Jan.) 1931. Hanlon, C. R., and Blalock, A.: Complete Transposition of the Aorta and the Pulmonary Artery, Ann. Surg. **127**:385 (March) 1948.

24. Haridas, G.: Aneurysm of Aorta with Complete Transposition, Brit. M. J. **1**:236 (Feb. 6) 1932.

25. Eakin, W. W., and Abbott, M. E.: Stenosis of Pulmonary Conus at Lower Bulbar Orifice (Conus a Separate Chamber) and Closed Interventricular Septum, with Two Illustrative Cases: Case 1, with Dextroposition of Aorta and Aneurysm of Interventricular Septum, All Fetal Passages Closed; Case 2, with Patent Foramen Ovale and Subacute Infective Endocarditis, Am. J. M. Sc. **186**:860 (Dec.) 1933.

26. Novikoff, A. S.: Transposition of Viscera with Roger's Disease: Case, Klin. Med. (no. 13) **7**:844 (July) 1929.

27. Bönniger, M.: Congenital Absence of Right Lung with Dextrocardia: Case in Adult, Med. Klin. **24**:258 (Feb. 17) 1928.

sinuses. Bronchiectasis, situs inversus and paranasal sinusitis, when occurring together, are referred to as Kartagener's triad,[28] 27 cases of which have been reported up to 1937. In the abdomen, transposition may be partial or complete, the latter being the most frequent. Some of the anomalies reported, other than partial or complete transposition, are dextrogastria,[29] atresia of the duodenum, polycystic kidney, absence of the spleen or multiple spleens, anomalous lobulations of the spleen, anomalous lobes and lobulations of the liver, including Riedel's lobe,[30] isolated situs inversus of the liver,[31] partial transposition of the upper abdominal viscera (liver, spleen, stomach and duodenum but not colon),[32] congenital obliteration of the bile ducts,[33] nonrotation of the colon, partial or total,[8] megacolon,[34] inversion of the colon below the splenic flexure [35] and congenital absence of the anus and rectum with a fistulous tract into the prostatic urethra.[36] Eighteen cases of cholecystitis associated with situs inversus have been reported up to 1939[1]; there have been 3 additional cases reported through 1946.[37] Appendicitis has

28. Kartagener, M.: Zur Pathogenese du Bronchiektasien, Beitr. z. Klin. d. Tuberk. **83**:489, 1933. Delp, M. H.: Kartagener's Triad: Situs Inversus, Absent Frontal Sinuses, with Maxillary, Ethmoid, and Sphenoid Infection, and Bronchiectasis, J. Kansas M. Soc. **47**:93, 1946. Richards, W. F.: Situs Inversus Viscerum, Absent Frontal Sinuses with Ethmoid and Maxillary Infection, and Bronchiectasis: Kartagener's Triad; Case, Tubercle **25**:27 (March-April) 1944. Adland, S. A., and Einstein, R. A. J.: Kartagener's Triad: Situs Inversus Viscerum, Bronchiectasis and Paranasal Sinusitis, Am. J. Dis. Child. **61**:1034 (May) 1941. Cole, D. B., and Nalls, W. L.: Situs Inversus, Sinusitis and Bronchiecasis, J. Thoracic Surg. **9**:689 (Aug.) 1940.

29. Varela de Seijas y Aguilar, J. R.: Dextrogastria with Megacolon: Pathogenetic Study of Case, Progrésos de la clín. **42**:22 (Jan.) 1934

30. Anton, J. I.; Panoff, C. E., and Spiegel, M. B.: Segmental Abdominal Heterotaxy: Situs Inversus Viscerum Abdominis Partialis, Am. J. Surg. **54**: 446 (Nov.) 1941.

31. Hammesfahr, C.: Isolated Situs Inversus of Liver: Case, Zentralbl. f. Chir. **58**:461 (Feb. 21) 1931.

32. Anton, Panoff and Spiegel.[30] Guttman, A. P., and Thompson, I. M.: Partial Transposition of Upper Abdominal Viscera, Canad. M. A. J. **54**:486 (May) 1946.

33. Smyth, M. J.: Congenital Obliteration of Bile Ducts with Total Transposition, Brit. M. J. **1**:84 (Jan. 18) 1941.

34. Acuña, M.; Casaubón, A., and Derqui, J. C.: Situs Inversus: Megacolon; Typhoid Fever, Semana méd. **2**:725 (Sept. 20) 1928.

35. Sasaki, K., and Kim, K.: Inversion of Colon Below Splenic Flexure: Case, Zentralbl. f. Chir. **59**:1514 (June 18) 1932.

36. Litvak, A. M., and Liveson, A.: Congenital Absence of Anus and Rectum with Fistulous Tract into Prostatic Urethra Associated with Dextrocardia: Case, Arch. Pediat. **54**:548 (Sept.) 1937.

37. Smyth.[33] Rossien, A. X.: Complete Heterotaxia Associated with Obstructive Jaundice, Canad. M. A. J. **46**:572 (June) 1942. Methany, D.; Sherwood, K. K., and Zimmerman, B.: Complete Situs Inversus Associated with Cholelithiasis, West. J. Surg. **50**:254 (May) 1942.

been reported twelve times in the past ten years.[38] Transposition may be familial [39]; it may occur in both of single ovum twins,[40] in siblings,[41] in newborn infants [42] and in a dwarf.[43] It has been observed in a person having three testicles [44] and has been associated with such orthopedic anomalies as congenital scoliosis and torticollis,[45] Köhler's disease and abnormal ossification,[46] congenital malformation of the vertebral column,[47] asymmetry of the brain and cranium and spinal curvature,[48] acrocephaly [49] and, in a case report submitted later in this article, spina bifida occulta and cervical rib. From the preceding material, it appears that the varieties of transposition are legion, the associated congenital anomalies are numerous and the person with situs inversus is as susceptible to acquired diseases as is one without it.

PATHOLOGIC ANATOMY

Wood and Blalock,[1] in summarizing Cleveland's description and photographic illustrations [4] of a cadaver with situs inversus totalis subjected to anatomic dissection, gave the following brief, but precise, description of the anatomic arrangements:

> The heart lies to the right of the midline, and its chambers are reversed, the apex being the right ventricle, from which arises the aorta. The aorta arches

38. Capone and Miller.[18] Levering, J. W.: Situs Inversus with Acute Surgical Abdomen, Clinics **4**:867 (Oct.) 1945. Prescott, M. U., and Zollinger, R. W.: Appendicitis in Situs Inversus Totalis: Cases, Am. J. Surg. **64**:288 (May) 1944. Lawrence, C. W.: Appendicitis with Complete Situs Inversus Viscerum (Case), J. Kansas M. Soc. **41**:333 (Aug.) 1940.

39. Natvig, H.: Familial Total Transposition, Nord. med. (Norsk mag. f. lægevidensk.) **1**:681 (March) 1939.

40. Kean, B. H.: Complete Transposition in Both of One-Egg Twins, J. Hered. **33**:217 (June) 1942.

41. Körner: Situs Inversus Totalis in Two Brothers, Röntgenpraxis **9**:197 (March) 1937.

42. Homma, H.: Situs Inversus Partialis in New-Born Infant: Case, Ztschr. f. Anat. u. Entwcklngsgesch. **102**:782, 1934.

43. Meyer, J. F.: Situs Inversus in a Dwarf, Am. J. Dis. Child. **48**:1080 (Nov.) 1934.

44. Soccorso, T.: Electrocardiogram in Case of Transposition of Viscera with Presence of Three Testicles, Folia med. **17**:752 (June 30) 1931.

45. Reuss, A.: Infant with Congenital Scoliosis, Torticollis and Dextrocardia, Wien. med. Wchnschr. **78**:29, 1928.

46. Gorianoff, R. V.: Congenital Isolated Transposition of Heart, Abnormality of Ossification and Köhler's Disease: Case, Vestnik roentgen. **6**:531, 1928.

47. Marinich, A. S.: Congenital Malformation of Vertebral Column with Total Transposition of Viscera, Ortop. i travmatol. (no. 4) **7**:62, 1933.

48. Spolidoro, F.: Asymmetry of Brain and Cranium and Spinal Curvature in Case with Complete Transposition, Sperimentale, Arch. di biol. **90**:588, 1936.

49. Marcos, J. R., and Mendivil, S.: Acrocephaly and Dextrocardia: Case, Arch. de pediat. d. Uruguay **10**:305 (May) 1939.

toward the right, giving off the innominate artery (which subsequently divides into the left common carotid artery and the subclavian artery), the right common carotid artery and the right subclavian artery. The great veins empty into the left atrium, whence the blood passes into the left ventricle, the pulmonary arteries, the pulmonary capillary bed, the pulmonary veins and the right atrium, respectively. The thoracic duct lies to the right and empties into the right subclavian vein near its junction with the internal jugular vein. The lungs are structurally reversed, the right being bilobed and the left trilobed. Intra-abdominally, the cardia lies to the right of the midline and the lesser curvature extends toward the left. The spleen is on the right, and the gallbladder and liver (with reversal of the normal lobular arrangement of the latter), on the left. The entire intestinal tract is reversed, with the cecum and appendix on the left and the sigmoid flexure of the colon in the right iliac fossa.

Partial transposition is known to occur in three main forms, although gradations between the types are so common as to make definite classification difficult. Thus, one may have partial transposition of both the thoracic and the abdominal organs, transposition affecting the abdominal organs alone, or dextrocardia alone.

CAUSE OF SITUS INVERSUS

Adams and Churchill [10] suggested that there may be two main types of persons having transposition of the viscera: first, the true mutant, in which the tendency toward transposition is inherited as a recessive character, the causal elements being in the germ plasm, and, second, the true monster, in which the transposition is the result of external influences acting on the developing embryo. Laboratory experiments on lower animals in which abnormal environmental influences, such as the use of chemical salts, variations in oxygen supply and lowering of the environmental temperature (thus reducing the rate of cellular oxidation), are brought to bear on the embryo, especially in the blastula and morula phases, tend to produce not only transposition, but also other unrelated anomalies. Changes are most likely to be produced when the abnormal environment is experimentally created during a stage in which there are decided inequalities in the rate of cellular proliferation in different parts of the embryo. Any one method may produce all types of monster and, conversely, any type of monstrosity may be produced by a great variety of methods. The end results appear to differ as to degree only, varying from very slight deviations from the normal to a true monster.

The mechanism by which situs inversus is produced in the human being has been explained in many ways. Cleveland [4] noted three views:

1. The persistence of a right omphalomesenteric vein influencing the shifting of the stomach to the right instead of to the left.

2. The influence of the umbilical cord. In situs inversus it is wound spirally to the right instead of to the left. The blood column flowing in the reverse direction is responsible for the turning of the heart to the opposite side.

3. The turning of the embryo to the right side of the umbilical vessels instead of to the left as it normally does.

DIAGNOSIS

The recognition of situs inversus totalis is based on finding the heart outline to the right of the midline, the apex impulse situated to the right, liver dulness on the left and stomach tympany on the right; in male subjects, the right testicle may be more dependent than the left. The diagnosis is confirmed by a roentgenologic examination of the gastrointestinal tract which shows the stomach to be on the right, duodenum on the left, liver shadow on the left, spleen shadow on the right, cecum and ascending colon on the left and descending and sigmoid colon on the right. Cholecystograms demonstrate a left-sided gallbladder and biliary tract. Electrocardiographic tracings reveal a total inversion of lead I and transposition of leads II and III.[50] The observations in situs inversus partialis vary from those of total transposition according to the degree of transposition present. The clue which leads to the ultimate diagnosis of situs inversus is most frequently the observation of dextrocardia. Displacements of the heart to the right may occur as a result of other lesions in the thorax pressing or pulling the heart out of its normal position and may be distinguished from true dextrocardia by means of the electrocardiogram or roentgenogram or by the identification of the displacing lesion. Similarly, a left-sided appendix may be due to an abnormally mobile cecum and must be distinguished from the left-sided appendix due to transposition.

Three cases of situs inversus totalis are reported herewith, 1 of which was associated with endometriosis, a cervical rib and spina bifida occulta.

REPORT OF CASES

CASE 1.—L. R., a 15 year old white school girl, was admitted to Norwegian-American Hospital on Sept. 8, 1946, complaining of pain and tenderness in the lower left abdominal quadrant. She had been quite well until nine months previously, at which time pain and tenderness with occasional nausea started and continued with gradually increasing severity until her admission to the hospital. She had lost about 5 pounds (about 2 Kg.) in the last two months. On September 7, roentgenologic examinations of her chest revealed dextrocardia and of her colon showed the cecum on the left side of the abdomen and the descending colon on the right. The appendix was broad and rather tender to pressure. A complete blood cell count at this time showed no abnormality except for a white cell count of 10,300. There were no complaints other than those given. She was right handed.

50. Waller, A. D.: On the Electromotive Changes Connected with the Beat of the Mammalian Heart and of the Human Heart in Particular, Phil. Tr. Roy. Soc., London **180**:169, 1889. Middleton, H. N.: True Congenital Dextrocardia with Situs Inversus Corroborated by Electrocardiographic and X-Ray Findings: Case, J. Indiana M. A. **30**:522 (Oct.) 1937. Parsonnet, A. E.: Complete Transposition with Electrocardiographic and X-Ray Studies: Case, Ann. Int. Med. **2**:963 (May) 1929. Rimbaud, L.; Serre, H., and Cohen-Tanugi, D.: Clinical, Radiologic and Electrocardiographic Studies on Total Transposition of Viscera, Montpellier méd. **21-22**:127 (March-April) 1942.

On physical examination she was observed to be of normal physical development, with no abnormalities except that the heart lay in the dextrocardiac position with the outlines reversed from the normal, the apex impulse being in the fifth interspace in the right midclavicular line. Liver dulness could be percussed on the left side, stomach tympany on the right and the liver edge felt at the costal margin on deep inspiration. The abdomen was tender and very slightly rigid in the left lower quadrant. Results of vaginal and rectal examinations were negative, except for some tenderness high in the left side. Results of urinalysis and blood cell count were negative except for a white cell count of 13,000 and a differential count of 62 per cent segmented neutrophils, 8 per cent band cells and 30 per cent lymphocytes. The reaction to the Friedman modification of the Aschheim-Zondek test was negative.

On September 9, with the patient under general anesthesia, through a left paramedian incision, the abdomen was explored: complete situs inversus abdominalis

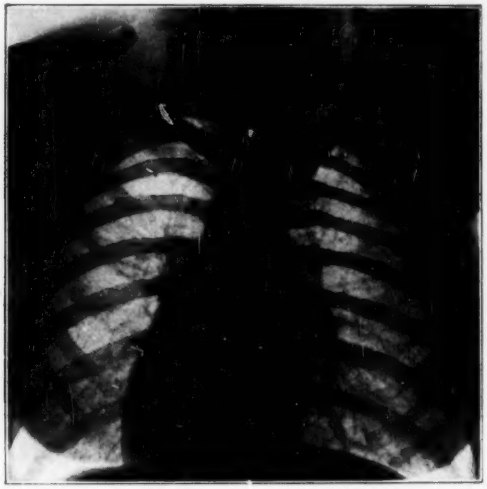

Fig. 1.—Roentgenogram of the chest, showing dextrocardia.

was seen, the liver being situated on the left, the stomach and spleen on the right, the appendix, cecum and ascending colon on the left and the descending and sigmoid colon on the right. The uterine cervix was hard and firm and the fundus uteri soft and somewhat boggy. The appendix was thick walled and fibrous, with fibrous adhesions to the serosa. A cyst in the left ovary measured 2 by 2 by 1 cm. in diameter and microscopically showed the characteristics of a corpus luteum cyst. The appendix and the cyst in the ovary were removed and the abdomen closed.

The patient was ambulatory on the fourth day and went home on the sixth postoperative day. She had remained well up to this writing.

Case 2.—L. F., a 27 year old white housewife, was admitted to the Hospital of St. Anthony de Padua on Sept. 7, 1947, complaining of pain in the lower part of the abdomen.

About ten days prior to admission she felt as though she were "catching cold"; she sneezed, and a severe pain suddenly occurred in the lower part of the abdomen, which persisted with increasing severity. It was diffuse and was aggravated by pressure and by urination. Since that time she had sharply restricted her food intake, because of the pain it caused. Three days before admission there was superimposed a diffuse pain or pressure sensation in the upper part of the abdomen, which radiated into the chest and both axillas, and, concurrently, though she previously had been habitually constipated, her bowel movement became loose. She had lost 7 pounds (about 3 Kg.) in the two months prior to admission.

Her health had been good until the onset of the present illness. A fractured patella, incurred eight months previously, had healed uneventfully. Three normal full term pregnancies had ended with normal spontaneous deliveries, the last of May 8. She had menstruated in July and August, with somewhat excessive

Fig. 2.—Roentgenogram showing the left cervical rib.

quantities on each occasion. A milky vaginal discharge followed the menses of August 24 and continued without change. She was right handed and was unaware of any congenital abnormalities among her blood relatives.

Complete physical examination disclosed no abnormalities except as follows: The teeth were badly decayed. Diaphragmatic excursions were diminished on both sides, and breath sounds were normal but diminished in volume. The heart was outlined to the right of the midline, and of normal size and shape, the apex impulse being in the right fifth intercostal space in the midclavicular line. Abdominal observations were moderate distention, more decided below the umbilicus, tympany in the right hypochondrium and dulness in the left, tenderness without rigidity in the lower part of the abdomen, normal peristaltic sounds and no signs of intraperitoneal fluid or mass.

Vaginal examination disclosed low grade cervicitis (erosion) in a transversely lacerated cervix, which was located in the anterior portion of the pelvic cavity.

There was limited mobility of the fundus uteri, which was in the cul-de-sac. There was decided, but not exquisite, tenderness and a sensation of increased resistance in both adnexal areas. Pain and muscle guarding prevented very deep palpation. Results of rectal and proctoscopic examinations were negative to a distance of 15 cm. from the anus.

A complete blood cell count revealed 11,600 white blood cells as the only noteworthy observation. No abnormalities were observed on examination of the urine.

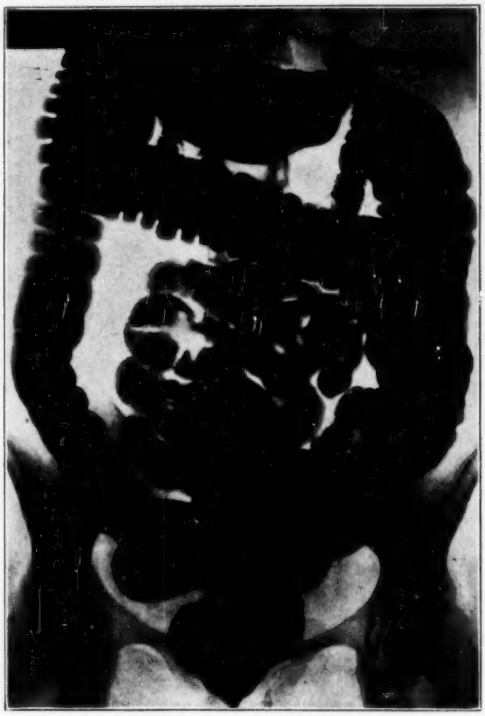

Fig. 3.—Roentgenogram of the gastrointestinal tract, with stomach, small intestines and colon simultaneously filled with barium sulfate for better demonstration. The cardia lies to the right of the midline, with the lesser curvature directed to the left. The duodenum, cecum and ascending colon are on the left and the descending colon and sigmoid on the right.

On September 8, with the patient under ethylene, oxygen and ether anesthesia, operation was performed. A midline incision from the symphysis pubis to the umbilicus was made and the abdomen opened and explored. Complete transposition of all the abdominal organs was seen. The liver was on the left, the stomach and spleen on the right and the pylorus and duodenum were to the left of the midline; the head of the pancreas was felt to the left of the vertebral column; the

cecum and appendix were on the left and the descending and sigmoid colon on the right.

The entire pelvis was matted with adhesions, some of which were old and puckered up from scarring. The fundus uteri was in the cul-de-sac, the size of a two and one-half month embryro, soft and boggy and normal pink. The right ovary measured 5.0 by 8.0 cm., contained many follicular and several endometrial cysts and was densely adherent to the broad ligament along the right side of the uterus, down to the level of the internal os. The left ovary was not remarkable except that its capsule was thick and fibrous. Both fallopian tubes were enlarged, had densely thickened white walls and varied from 1.5 cm. to 2.0 cm. in diameter. The fimbriated extremities of both tubes were densely adherent to adjacent tissues. On the left side of the lower part of the abdomen and pelvis there was a large organized blood clot, with dense fibrous infiltration and firm fibrous adhesions attaching it to the broad ligament, the fimbriated extrem-

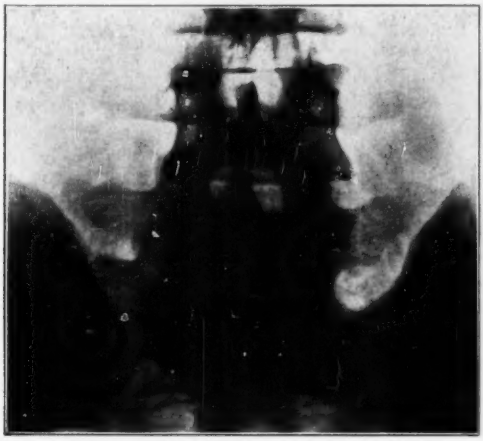

Fig. 4.—Roentgenogram of the lumbosacral part of the spine, showing spina bifida occulta of the first sacral segment with a slight rotation to the right of the fifth lumbar vertebra and the first sacral segment.

ity of the left fallopian tube, a portion of the more mobile part of the rectosigmoid, the distal third of the appendix and a portion of the cecum and terminal ileum. Endometrial plaques were growing on all these tissues except the appendix, no deep penetration of the walls of the intestines nor distortion of their continuity being observed. The largest single endometrial implant observed measured 2.5 by 4.5 cm. The tip of the appendix appeared to be lying in a small fibrinous cavity, as though it had at some previous, but not recent, time been involved in a periappendical abscess, the fluid contents of which had since been absorbed.

The adhesions were freed and normal anatomic relationships restored. The appendix was removed and the stump inverted. Both fallopian tubes and ovaries were removed, together with the hematoma on the left. The fundus uteri was

returned to its normal anterior position and anchored to the round ligaments. Bleeding was controlled, peritoneal toilet performed and 100,000 units of penicillin in isotonic sodium chloride solution and 5.0 Gm. of crystalline sulfathiazole were distributed over the operative area. Omentum was used to cover endometrial implants in the ileum and colon and to overlay the pelvic organs. The abdomen was closed without drainage.

The report submitted by the pathologist confirmed the observations.

Shock set in one hour after the onset of the operation, the systolic blood pressure dropping from a preoperative level of 110 mm. of mercury to 73 mm. of mercury. Parenterally administered fluids and a transfusion of 500 cc. of citrated blood brought the systolic blood pressure back to its preoperative level, but not until four hours had elapsed. Parenteral administration of fluids was continued; a second transfusion of 500 cc. of citrated blood was given on September 10. The temperature reached 101 F. on the second postoperative day and returned to normal on the third day. Penicillin therapy, 25,000 units, given

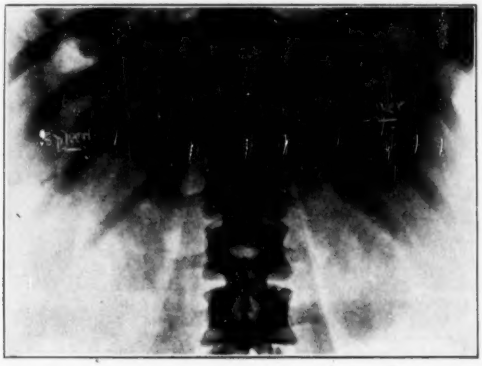

Fig. 5.—Roentgenogram showing the shadow of the liver on the left and the shadow of the spleen on the right.

intramuscularly every three hours, started on admission, was stopped on the fifth postoperative day. Examination of the blood on September 13 showed hemoglobin 10.5 Gm. (67 per cent) and erythrocytes 4,020,000 per cubic centimeter. She was actively moving in bed from the first day, was ambulatory on the fifth day and was discharged from the hospital on the ninth day. On December 5, her hemoglobin had risen to 13.5 Gm. (81 per cent) and her erythrocyte count to 4,050,000 per cubic centimeter.

She menstruated heavily in October, for three days in November, for five days in January and for five days in March, each time profusely, after which menopause was induced by roentgen irradiation.

A roentgenologic study of her chest (fig. 1) showed dextrocardia and a left cervical rib (fig. 2). A similar study of her gastrointestinal tract (fig. 3) demonstrated a complete transposition of the abdominal viscera and a spina bifida occulta of the first sacral segment (fig. 4), with a slight rotation to the right of the fifth lumbar vertebra and the first sacral segment. The shadow of the liver was on the left and the shadow of the spleen on the right (fig. 5). Electro-

cardiograms (fig. 6) disclosed a complete inversion in lead I of all its complexes. Leads II and III were reversed from the normal order. The axis deviation was to the right. The chest leads CF_1, CF_2 and CF_4 had negative T waves. No significant deviations from the normal were noted; the observations were those of dextrocardia.

Case 3.—J. S., a 38 year old white milk deliveryman, was referred to Norwegian-American Hospital on Jan. 12, 1948, by Dr. S. T. Bolstead, complaining of "piles," pain on bowel movement and blood-streaked stools for one year. He was treated with injections about one year prior to admission, without much benefit. He stated on admission that his heart was on the right side and his appendix on the left, having been so informed during the course of a physical examination by his physician who, in a personal communication to me,[51] stated that fluoroscopy in 1938 divulged this information and also showed his stomach

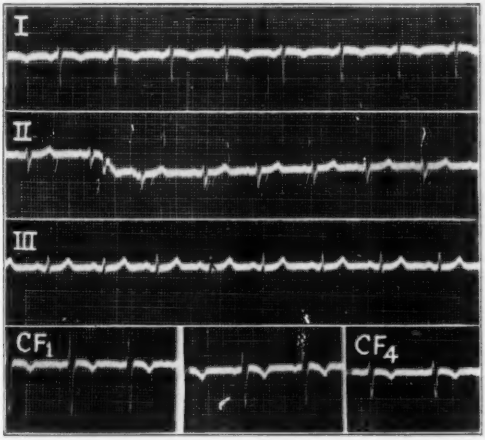

Fig. 6.—Electrocardiogram showing inversion of lead I, reversal of leads II and III and negative T waves in leads CF_1, CF_2 and CF_4, with right axis deviation. Essentially observations were normal except for reversal, a characteristic pattern for dextrocardia.

to be on the right side of his abdomen and that inspection disclosed the right testicle to be more dependent than the left. The history and results of physical examination were otherwise negative except that the right border of the heart was in the right midclavicular line, the left border 1 cm. to the left of the sternum and the apex impulse in the sixth right intercostal space in the midclavicular line. Examination of the external genitalia demonstrated bilateral varicoceles. Internal and external hemorrhoids were noted. On January 13, a hemorrhoidectomy was performed by the cautery method with the patient under nitrous oxide and ether anesthesia. His postoperative course was uneventful, and he was discharged on January 17 in good condition.

51. Bolstead, S. T.: Personal communication to the author, 1948.

SUMMARY

Situs inversus has been known from antiquity; it is far commoner than has been generally recognized, over 1,000 cases having been recorded; it may possibly occur in the general population as often as, or even more often than, 1 case in 1,379 persons. It varies greatly in the number of organs involved and their degree of involvement, is frequently associated with other congenital anomalies and is at least as frequently associated with any acquired disease as is situs normalis. *Per se,* it is not incompatible with normal health. Transposition is believed to be caused by either a defect in the germ plasm or some deleterious environmental influence acting on the developing embryo.

The recognition of situs inversus can usually be made on physical examination: the heart is situated to the right of the midline; tympany of the stomach is detected on the right and dulness of the liver on the left, and, in male subjects, the right testicle may be more dependent than the left. Electrocardiograms and gastrointestinal roentgenograms confirm and elaborate on the diagnosis.

Three cases of total transposition of the viscera are presented, in 1 of which there were other skeletal anomalies, namely, a cervical rib and spina bifida occulta.

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EFFECT OF HEPARIN AND PENICILLIN ON EXPERIMENTALLY PRODUCED THROMBOPHLEBITIS

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EXPERIMENTAL evidence was produced in a previous report[1] to show that heparin would prevent the formation or cause the solution of an intravascular clot. It was also shown that heparin was particularly effective as an anticoagulant when administered to the animal both prior to and immediately after the formation of the clot. Heparin was of no effect when given several days after the formation of the clot, when the latter was partly or completely organized.

The present study was undertaken with the view of determining whether heparin alone, or in combination with penicillin, could bring about the solution of a clot in the presence of experimentally produced, acute thrombophlebitis. It was surmised that the action of the drug would be different in the presence of an acute inflammatory process in the vein than in normal circumstances. Two problems confronted us in this study: first, would the administration of heparin prevent the formation or cause the solution of a locally produced, infected intravascular clot if given prior to or immediately after the formation of the thrombus; and, second, would heparin in combination with penicillin prevent or cause the solution of, such a clot? On this basis, the following experiments were carried out.

PRESENT STUDY

Control Experiments.—In the following series of experiments a clot was produced in the jugular veins of 10 rabbits according to the technic described in a previous communication. Briefly, the procedure may be described as follows: With the animal under ether anesthesia and with a sterile operative technic, an incision was made in the midline of the neck, and both jugular veins were exposed

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1. Rabinovitch, J., and Pines, B.: The Effect of Heparin on Experimentally Produced Venous Thrombosis, Surgery **14**:669, 1943.

and freed from the surrounding tissues for a short distance. The veins were then traumatized by a forcible pull applied at each end of the liberated vein. A localized clot formed almost invariably after such trauma to the vessel. The formation of the clot was further aided by narrowing the lumen of the vessel with a constricting ligature, care being taken not to obliterate the lumen completely, and a free, although retarded, flow of blood being allowed through the narrowed vein.

In the present experiments, in addition to traumatizing the vein, a few drops of a fairly virulent culture of Staphylococcus aureus suspended in isotonic solution of sodium chloride were injected into the vessel wall, great caution being taken not to introduce the culture into the lumen of the vessel. The animals were allowed to recover from the operation, and two days later the wound in the neck was reopened and the veins were examined. It was observed at this time that the traumatized veins were acutely inflamed and that the inflammatory process had spread to involve the surrounding soft tissues of the neck. The lumen of the vein in each instance was observed to be occluded with a freshly formed clot, which could be readily palpated, or visualized when the vessel was sectioned. A portion of the vein bearing the clot was removed for further microscopic study.

Microscopic examination of the veins showed the characteristic picture of acute thrombophlebitis. The walls of the vessels were edematous and densely infiltrated with inflammatory cells, particularly polymorphonuclear leukocytes. These cells were often disintegrated and showed conspicuous pyknotic changes. In a number, there was evidence of tiny abscess formation within the vessel wall. The lumen of the veins was occluded with a thrombus, composed of a fibrinous network in which were enmeshed all the cellular constituents of the blood, particularly the polymorphonuclear leukocytes. The unusually large collection of leukocytes in the clot was striking and at once suggested the presence of an acute inflammatory process (fig. 1). Almost invariably, the very same picture was observed in each of the control experiments.

Effect of Heparin.—In the following series of experiments, acute thrombophlebitis of the jugular veins was produced in 6 rabbits according to the technic described for the controls. Two days later, the wound in the neck was reopened and the veins were examined for the presence or absence of thrombophlebitis. When both veins were observed to be thrombosed, a portion of the vein bearing the clot was removed for microscopic examination and served as a control. The constricting ligature was removed from the other vein which was otherwise left undisturbed. The animals were then given daily injections of heparin

in amounts sufficient to keep the circulating blood fluid for a period of five to seven days. At the end of this time the animals were operated on again and the other jugular vein removed and examined.

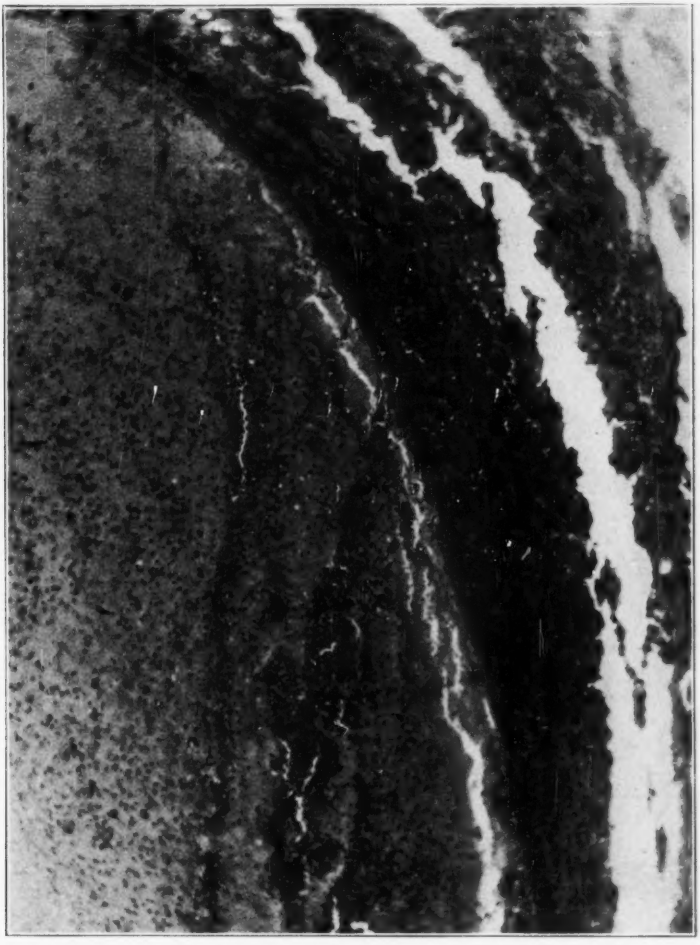

Fig. 1.—Acute thrombophlebitis, showing acute inflammation of the vessel wall. The lumen of the vein is occluded by a thrombus (control experiment).

Grossly, the vein still presented evidence of an acute inflammatory process, and the lumen was occluded with a thrombus. Microscopically,

the vein presented a typical picture of acute thrombophlebitis, which was indistinguishable from that of the control (fig. 2). The vessel wall was edematous and densely infiltrated with polymorphonuclear leukocytes. Occasional areas of necrosis with miliary abscess formation

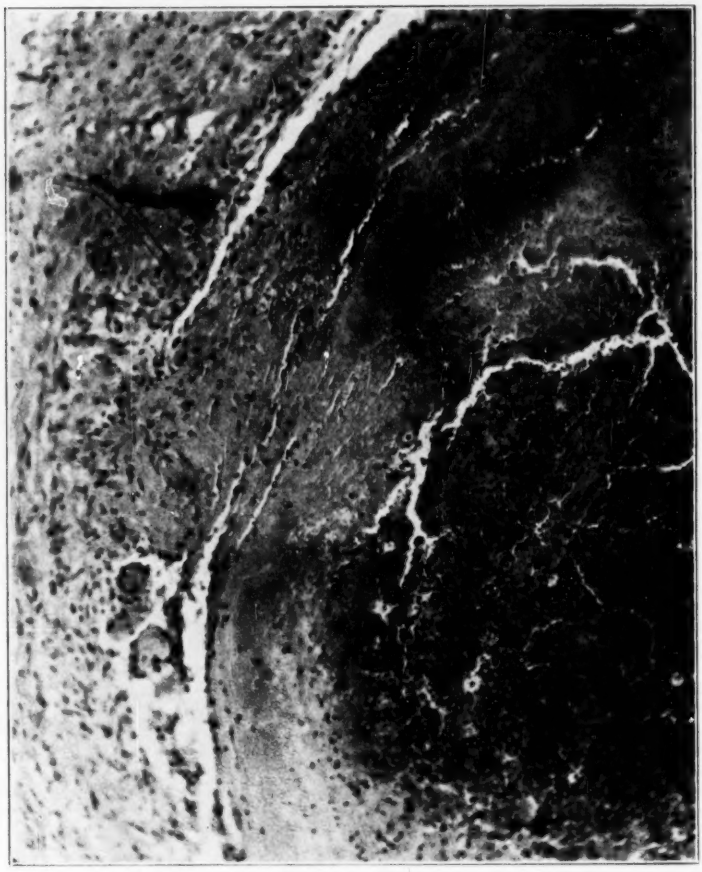

Fig. 2.—Jugular vein of an animal which received preoperative and postoperative injections of heparin. Note the existence of an acute thrombophlebitis.

were also noted. The lumen of the vessel was completely occluded by an adherent fibrinous clot, which, again, showed a striking predominance of poylmorphonuclear leukocytes. It was evident from a study of the

specimens that heparin was entirely ineffective in causing the solution of the clot or in altering its characteristic structure.

Since in these experiments heparin was not administered to the animals until two days after the formation of the clot, it seemed possible that certain changes might have occurred in the clot at this time which caused it not to respond favorably to the anticoagulating effects of the drug. For this reason, an additional series of experiments was carried out with the purpose of administering the heparin immediately after traumatizing the vein and inoculating it with the bacterial culture. Therefore, the heparin was given to the animals prior to the development of the acute thrombophlebitis and for a period of five to seven days thereafter. At the completion of heparin therapy, the animals were operated on again and the veins examined.

Gross examination of the veins revealed the presence of acute thrombophlebitis in each of the 6 animals used in this experiment. The gross observations were also corroborated by microscopic study, which again revealed evidence of acute thrombophlebitis, similar in character and appearance to that noted in the controls. It is evident, therefore, that under these experimental conditions heparin can neither prevent the formation of a thrombus when administered prior to its development nor cause the solution of the clot when given for several days after its formation. It appears, then, that the action of heparin as an anticoagulant in the presence of acute thrombophlebitis is entirely different from that seen in an uninfected clot. We have shown in previous experiments that heparin will prevent the formation of a simple traumatic clot if administered before the clot forms, and that it will cause the solution or disappearance of a similar clot if administered in the early stages of its formation. It is difficult to explain this difference in behavior of heparin under the two experimental conditions unless it is assumed that some, as yet unexplained, factor or factors come into play in the case of acute thrombophlebitis which render heparin ineffective as an anticoagulant, and which are absent in the case of simple traumatic thrombosis.

Effect of Combined Administration of Heparin and Penicillin on Acute Thrombophlebitis.—In the following series of experiments, the animals were given injections of heparin and penicillin, and their combined effect on clot formation was noted. In 12 rabbits, acute thrombophlebitis of the jugular veins was produced according to the technic described for the controls. Immediately prior to the operation, and for a period of seven days thereafter, the animals received daily injections of 200,000 units of penicillin intramuscularly and of heparin intravenously. At the end of this time, the veins were examined. It was then observed that 6 of the animals so treated showed no gross or microscopic evidence of thrombus formation. The vessel wall,

Fig. 3.—Jugular vein of an animal which received a combination of heparin and penicillin. Note the absence of clot in the lumen and the presence of an inflammatory process in the vessel wall.

however, was still the seat of an acute inflammatory process, although to a less severe degree than that in the controls (fig. 3). In 2 other animals, the lumen of the vessel was only partially occluded with a loose, retracted clot, which consisted largely of agglutinated erythrocytes, with very little fibrin and few leukocytes. In the remaining 4 animals there was still evidence of acute thrombophlebitis. It is evident, therefore, that the combined action of heparin and penicillin will prevent the formation or cause the solution of an infected thrombus in at least 50 per cent of cases. It may be added, also, that the solution of the thrombus occurs in spite of the fact that the inflammatory process in the vessel wall persists. It is questioned whether a more prolonged administration of the two drugs would eliminate the clot in the remaining cases. Such questions require further investigation.

COMMENT

The results obtained in these experiments demonstrate clearly that heparin will not prevent the formation of an intravascular clot in the presence of an acute inflammatory process in the vein, nor will it cause the solution of such a clot under similar pathologic conditions. It is apparent that some, as yet unexplained, factor or factors come into play in the case of acute thrombophlebitis which render heparin ineffective as an anticoagulant. In previous experiments we demonstrated conclusively that heparin is a potent anticoagulant, capable of preventing the formation of a simple clot if administered to the animal before the clot is allowed to form. Heparin was also shown to cause the solution or disappearance of a thrombus already formed if injected in sufficient quantities in the early stages of the clot formation. This difference in action of heparin on a simple clot and on an inflamed one is striking and of considerable practical significance. These experimental findings suggest that heparin is effective as an anticoagulant in the case of simple phlebothrombosis, but is of no value in the case of acute thrombophlebitis.

The simultaneous administration of heparin and penicillin to animals with acute thrombophlebitis yielded entirely different results. In at least 50 per cent of the animals the combined use of heparin and penicillin either prevented the formation or caused the disappearance of the thrombus. In approximately 16 per cent there was partial solution of the clot, and in the remaining 34 per cent the drug had no effect on the thrombus formation. Of particular interest is the fact that in the animals in which the drugs were effective in causing the solution or disappearance of the thrombus, the vessel wall remained acutely inflamed, although to a less pronounced degree than that seen in the control. The question arises now: How does the combined administration of heparin and penicillin effect the solution of the thrombus?

One of the most interesting facts disclosed in the experimental studies of recent years is the observation made by Nathanson and Liebhold,[2] who showed that penicillin possesses the unique power of being able to permeate fibrin. On the basis of these experiments and the pathologic observations described, we are inclined to believe that penicillin, when administered, permeates the fibrin in the clot and inhibits the growth and activity of the organisms responsible for the acute thrombophlebitis. Once the bacteria have been rendered inactive by the penicillin, heparin can then act freely in dissolving the clot. Such an assumption will also explain the fact that, although the clot disappears from the lumen of the vein, the vessel wall may remain acutely inflamed. It is also evident that, in order for penicillin to be effective in its action, it must be given in sufficiently large quantities and for a sufficiently long period.

The experimental evidence presented has a practical application, and the importance of these observations requires little comment. Sufficient data have been accumulated from this study, and from those of other investigators, to permit the conclusion that the combined administration of heparin and penicillin will cause the solution or disappearance of a clot in a fairly large number of cases of thrombophlebitis, especially if given in the early stages of the clot formation. Furthermore, heparin alone is of no value in preventing the formation of or in causing the solution of a clot in the presence of acute thrombophlebitis.

SUMMARY

Experimental evidence has been produced to show that heparin is not effective in preventing the formation of or causing the solution of an intravascular clot in the presence of acute thrombophlebitis.

The combined administration of heparin and penicillin will prevent or cause the disappearance of a clot in a large number of subjects with experimentally produced acute thrombophlebitis.

Roche-Organon, Inc., Roche Park, Nutley, N. J., supplied the heparin used in these experiments.

555 Prospect Place.

2. Nathanson, M. H., and Liebhold, R. A.: Diffusion of Sulfonamides and Penicillin into Fibrin. Proc. Soc. Exper. Biol. & Med. **62**:83, 1946.

FACTORS CONTRIBUTING TO LOW MORTALITY FROM APPENDECTOMY FOR ACUTE APPENDICITIS

A Ten Year Study

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IN SPITE of gradual, steady improvement in operative mortality reported by numerous authors, the treatment of acute appendicitis remains one of the most serious and frequent problems confronting the surgeon. The 6,697 persons listed in the latest available United States census reports as dying of appendicitis in this country in 1945 indicate that there is still need for efforts to improve our methods of dealing with this disease and to widen their effective use. As one such effort, the experience of our clinic with acute appendicitis for the ten year period 1938 through 1947 has been reviewed in an effort to seek lessons that may continue to be applied toward holding the mortality rate among patients treated for this disease at or close to the zero point.

CLINICAL MATERIAL

Numbers and Types of Cases.—During the ten years from January 1938 through December 1947, 1,411 patients underwent operation at Henry Ford Hospital, Detroit, for acute appendicitis. For 1,365 patients (97 per cent) the operation was appendectomy. For 46 (3 per cent) it consisted of simple drainage of an appendical abscess without appendectomy. One fourth of the removed appendixes revealed gangrene; 28 per cent of the gangrenous appendixes revealed perforation. These are the laboratory findings, based on gross and microscopic examination.

The over-all hospital mortality for the entire series was 0.64 per cent (9 deaths). All 9 deaths occurred during the first five years of the decade, a mortality rate of 1.1 per cent (824 patients). Among the remaining 587 patients operated on since 1942 the mortality rate was therefore zero. Among the 46 patients who had abscesses drained there were 2 deaths, a ten year mortality rate of 4.4 per cent. Among all 1,365 patients who underwent appendectomy there were 7 deaths,

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a ten year mortality rate of 0.5 per cent. These figures are summarized in table 1.

Clinical Findings.—From the standpoint of diagnosis, the incidence and grouping of symptoms, physical signs and laboratory evidence of acute appendicitis in this series of cases showed no important deviation from those long recognized as characteristic of that disease and are here cited only in part and in the briefest fashion.

According to the patients' histories on their admission to the hospital, 31 per cent of them had had previous attacks, and 20 per cent had used cathartics; 75 per cent complained of nausea as an early symptom,

TABLE 1.—*Postoperative Mortality of Acute Appendicitis*

Procedure	Five Years 1938 to 1942			Five Years 1943 to 1947			Ten Years 1938 to 1947		
	Total	Died	%	Total	Died	%	Total	Died	%
All operations	824	9	1.1	587	0	0	1,411	9	0.64
Appendectomy	806	7	0.9	559	0	0	1,365	7	0.5
Abscess drained	18	2	11.0	28	0	0	46	2	4.4

TABLE 2.—*Duration of Symptoms*

Duration	Per Cent of All Cases
Within 12 hr.	29.0
12 to 24 hr.	30.5
24 to 36 hr.	11.5
36 to 48 hr.	11.5
48 to 60 hr.	2.0
60 to 72 hr.	6.2
4 days	2.9
5 days	2.0
6 days	0.5
7 days	2.5
Over 7 days	1.4

59 per cent of vomiting, 13.5 per cent of diarrhea and 13.8 per cent of constipation. Forty-five per cent had generalized abdominal pain at the onset of their attack, 25 per cent pain confined to the right lower quadrant, 12.5 per cent epigastric pain and 8.5 per cent periumbilical pain. There was a shift of pain to the right lower quadrant in 62 per cent.

The duration of symptoms before admission is shown in table 2.

On examination of the patients on their admission to the hospital, localized tenderness in the right lower quadrant was found in 97 per cent, muscle spasm in 65 per cent and rebound tenderness in 73 per cent.

The total leukocyte count lay between 10,000 and 20,000 in 71 per cent of cases. The relative proportion of counts above and below these figures were approximately equal. The proportion of polymor-

phonuclear leukocytes ranged from 81 to 90 per cent in half the cases. In the other half there was a slight preponderance of lower counts.

Nonfatal Complications.—There were sixty-three nonfatal postoperative complications, recorded under fourteen headings. They represent an incidence of 4.5 per cent and are shown in table 3.

A number of the items in this table require brief comment. The incisional abscesses are those occurring in wounds closed without drainage. They were all small and of short duration. Shallow wound separations without evisceration occurred in 3 cases in which drained McBurney incisions were used and in 1 in which there was a drained transverse incision in the lower abdominal area. An incisional hernia occurred in a case in which a right rectus incision was made and in 12 cases in which drained McBurney incisions were used. All were of the small, buttonhole type. Two fecal fistulas followed inversion, and

TABLE 3.—*Nonfatal Complications*

Complication	Number	Per Cent Incidence
1. Incisional abscesses (all minor)	12	1.13
2. Wound separations (all small)	4	0.28
3. Incisional herniae (all small)	13	3.6*
4. Intra-abdominal abscesses	11	0.8
5. Fecal fistulas (nonpersisting)	3	0.21
6. Pneumonia	8	0.57
7. Atelectasis (massive)	2	0.14
8. Pulmonary embolus	2	0.14
9. Phlebothrombosis (femoral)	3	0.21
10. Acute parotitis	1	0.07
11. Acute pyelitis	1	0.07
12. Acute hepatitis	1	0.07
13. Empyema thoracis	1	0.07
14. Bronchial fistula	1	0.07

* This figure was calculated from only the 305 cases in which wound drainage was used.

one followed simple ligation of the appendical stump. All three healed promptly and spontaneously.

Ten postoperative, nonfatal pulmonary complications occurred, an over-all incidence of 0.71 per cent. There were 8 cases of pneumonia and 2 of atelectasis. Inhalation anesthesia was used for eight operations and spinal anesthesia for two, but the incidence figures for the number of times each type was used were nearly equal, 0.69 per cent and 0.79 per cent respectively. We are doubtful if any markedly different choice or distribution of anesthetic agents would have lessened this small number of pulmonary complications.

Postoperative Mortality.—Death followed operation in 9 cases, as shown in table 4.

The 5 deaths from generalized peritonitis were all results of continued overwhelming infection and require no special comment.

The patient with pulmonary embolus, a man of 63, died suddenly on the sixth postoperative day, without warning and apparently of his first embolic episode.

Another elderly man of 64, who gave an antecedent history of myocardial disease, died suddenly on the second postoperative day of symptoms clinically resembling those of coronary occlusion. Permission for autopsy was not obtained.

The presence of Addison's disease in 1 patient was known before the operation for appendicitis with perforation and spreading peritonitis was undertaken. An addisonian crisis developed on the day after operation.

The death from cerebrospinal meningitis occurred actually three years after appendectomy. It was, however, the culmination of a chain of tragic complications so clearly related one to another that it should not be excluded from the mortality list. During the seven weeks of his original stay in the hospital the patient had a pelvic abscess, a subphrenic abscess, empyema and a bronchial fistula. Subsequently he required treatment for chronic intraperitoneal abscesses, a renobronchial fistula, pyonephrosis (nephrectomy) and osteomyelitis.

TABLE 4.—*Causes of Postoperative Deaths*

	Following Appendectomy	Following Drainage Only
Generalized peritonitis	3	2
Pulmonary embolus	1	0
Probable coronary occlusion	1	0
Addisonian crisis	1	0
Cerebrospinal meningitis	1	0
Total	7	2

COMMENT

Diagnostic Principles.—Acute appendicitis is so common and so serious a disease that its early recognition places great and pressing responsibility on the surgical consultant. Belief in the slogan, "Never forget to play appendicitis against the field," in the consideration of any acute abdominal disease was shared by all staff surgeons participating in this series of operations and taught each of the many residents working under their supervision. Whatever the time of day or night, no pains were spared or inconvenience avoided in using promptly every help that careful history taking, methodical examination and pertinent laboratory tests could bring to bear on the diagnosis of symptoms or signs by any chance ascribable to appendicitis.

Prompt Operation.—When a diagnosis of acute appendicitis was made, exactly the same attitude motivated a policy of proceeding to operate promptly on all patients judged able to withstand operation, regardless of the presence of perforation. Eighty-eight per cent of the appendectomies were treated as emergencies. In only 12 per cent of the

series was deliberate delay allowed. For the most part, the delay was of only a few hours' duration and was used to combat severe dehydration and/or disturbance of blood chemistry. Expectant treatment of the Ochsner type was used only in 2 per cent of patients, whose debility was of such a degree that it made the risk of immediate operation forbidding. It is believed that consistent adherence to the principle of prompt surgical intervention for acute appendicitis has played an important favorable part in the results of this series of operations and that delay or compromise, for example in favor of chemotherapy, will tend to jeopardize the attainment of equal results in future series of comparable size.

Anesthesia.—Inhalation anesthesia was used in 81.5 per cent of the 1,411 operations and spinal anesthesia (procaine) in 18 per cent. Local anesthesia alone was used only five times in the entire series, and intravenous anesthesia was not used at all. For adults and adolescents, anesthesia was of the gas-oxygen type, with ethylene preferred as the agent. Cyclopropane or ether was often used as a supplement and occasionally as the primary agent. Nitrous oxide was not favored. For children and infants, open drop ether was the anesthetic of choice.

Inhalation anesthetics were administered by trained nurse anesthetists of the operating room staff, each assuming her share in rotation of emergency night duty. Spinal anesthesia was given by the operator or his assistant.

The preference for inhalation anesthesia is attributable to a belief in its somewhat greater safety and range of application rather than to misgivings regarding spinal anesthesia. The use of inhalation anesthesia does not require the oftentime consuming evaluation of risk demanded by spinal anesthesia, and, with the operative technic used, the greater relaxation obtainable with spinal anesthesia is not indispensable. Furthermore, the recent introduction of safe preparations of curare has brought the degree of relaxation possible under inhalation anesthesia almost to that possible with spinal anesthesia.

The Steps of Operation.—The attitude of this clinic toward appendectomy as toward other operations has been consistently that of the Halsted school of surgery. Although many surgeons participated in these operations, there was a decided uniformity in the incision chosen and in the technical manipulations employed for exposure and removal of the appendix. No single step in the operation originated with us, but a pattern of procedure has been established which we have found adequate for avoiding the pitfalls inherent even in "easy" appendectomies and helpful in surmounting the difficulties so often encountered. We believe that some of the steps are of such great importance for consistent good results that they deserve brief mention.

The McBurney incision was used in 93 per cent of all operations. Of the advantages of this incision which are numerous, important and generally recognized, two deserve special emphasis. One is that the location of the incision and the limited exposure increase the necessity for the most painstaking and accurate preoperative diagnosis. The second is that the same factors of location and size discourage meddlesome manipulation and harmful exploration during operation. In our series it was only occasionally necessary (3.8 per cent of cases) to amplify the exposure of a McBurney incision by means of a Weir (cutting transversely the exposed lateral edge of the rectus fascia) extension.

After the incision, the next point considered of great importance is the method used for identifying and delivering the appendix. As soon as the peritoneum is opened, it is the practice in this clinic first to identify and expose some portion of the cecum and not to feel first for the appendix itself, however tempting the latter procedure may be. As soon as a bit of the cecal wall comes into view, one of its longitudinal muscle bands is used as the invariable and unfailing guide to the base of even the most obscurely buried appendix. If the cecum is reasonably mobile, a free-lying appendix will come into sight and up into the wound without difficulty. If, on the other hand, the cecum is not freely mobile or the appendix is held by adhesions or is in an unusual location, primary identification of the appendical base secures, with minimal intra-abdominal manipulation, that part of the organ which must ultimately be dealt with in the act of removal. To this end, a short length of moistened half-inch (1.27 cm.) cotton tape is passed through the mesoappendix close to the cecum and by gentle traction brings and keeps the cecum under control with minimum trauma. Gentle exploration with the finger and any necessary blunt or sharp dissection can then be carried out methodically from a known point of departure. It is occasionally necessary to mobilize a fixed cecum by incising its lateral peritoneal reflexion for a short distance.

The next step needing emphasis is control of the vessels of the mesoappendix. Mass ligation was discouraged because in the difficult case a slipped or broken ligature may lead to disaster. Instead, individual ligation of the main mesoappendical branches was practiced. This more than any other step in the operation called for the most precise teamwork between operator and assistant.

The next point for emphasis is the method of amputation. Inversion of the appendical stump was practiced in 96 per cent of the appendectomies of this series. In 4 per cent inflammatory indurations of the cecum made inversion impossible. For inversion, a purse-string suture was used and was always placed before the proximal end of the appendix was crushed and ligated. The material of the suture and the method

of its placing were considered matters of prime importance. The preferred material was fine silk on a fine, straight sewing needle or a curved, split-eye needle. The suture commenced and ended on the antimesenteric side of the appendical base. Five bites sufficed, and each bite was aimed to pierce the serosal and muscular coats of the cecum perpendicularly, pick up the tough submucosa but neither enter nor pierce the mucosa. The first and last bites of the suture were not closer than 1 cm., and the purse string surrounded the base of the appendix at the shortest distance permitting inversion in the individual case.

The practice of "walling off" by stuffing Mikulicz or other gauze sponges through the wound into the abdomen was discouraged.

The last point to be mentioned in connection with operation is drainage. Drainage was used in our cases whenever there was grossly recognizable pus in the peritoneal cavity, either free or walled off. The watchword "when in doubt, drain" was accepted. The standard material for drainage was soft rubber dam, sometimes of the "cigaret" type but more often not. Rubber tubing or catheters were never used. Drainage was carried out in 25 per cent of the 1,411 cases. In 22 per cent of the cases drainage accompanied appendectomy, and in 3 per cent drainage alone was employed.

The Operating Surgeon.—One hundred and one surgeons participated in this series of operations, but 16 of them performed two thirds of the operations. Six of the 16 were full time staff surgeons, eight were head residents and two courtesy staff members both of whom had received their surgical training at the hospital. None of the sixteen performed less than twenty-five operations, and half of them performed more than fifty operations. The remaining one third of the operations was distributed among 8 full time staff surgeons, 8 of the courtesy staff and 69 junior residents. It seems of great significance to us not only that the larger portion of the operations were done by a relatively few experienced men but also that every other participating surgeon received his training in the same school of surgical thought and practice and performed his operations according to a rather uniform and consistent pattern of technic.

POSTOPERATIVE TREATMENT

Sulfonamide Compounds and Antibiotics.—Of all the therapeutic agents available during the past ten years as supplements to surgical treatment, the sulfonamide drugs and the antibiotics have been unquestionably the most important. Limited at first, both in availability and variety, they were administered to only 6 of the 320 patients with acute appendicitis seen in the years 1938 and 1939. Thereafter, especially after the development of sulfadiazine, these drugs were used with

increasing frequency until 1943. After that they were used less often, until they were virtually replaced by penicillin in 1947. Twenty-two patients received sulfonamide drugs intraperitoneally as well as by other routes, 46 received them intraperitoneally only and 196 received them only by the oral or the parenteral route. It is clear from a review of the case histories that the sulfonamide drugs were used throughout with discrimination and always with great respect for their potential dangers. Fortunately, no serious adverse effects were encountered.

Penicillin was released for general use only in late autumn of 1945. Nevertheless, it was used in connection with two thirds of the operations done in the last three months of that year and in over half of the 228 operations of 1946-1947. Due to its negligible toxicity and its spectacular efficacy, penicillin has been used with much less restraint than the sulfonamide compounds. Its beneficial effects in seriously ill patients have been too obvious and striking to need detailed description.

The incidence of nonfatal complications before penicillin became available was slightly in excess of that after its use began, 4.8 per cent compared with 3.6 per cent, but the mortality rate had already been zero for two years before penicillin came into use.

Streptomycin, still more recently released for general use, was employed in only 11 cases, all in the year 1947 and each time in conjunction with penicillin. Its additional benefit, though presumed, is not easily demonstrable from those few cases.

Nutrition, Water, Electrolytes and Blood.—The fact that only brief mention is made here of diet, fluid intake and maintenance of electrolyte balance does not in any way discount the great importance which we attach to those factors in postoperative care. Parenterally administered fluids serving various purposes and often blood were freely used when it seemed necessary, but the great majority of patients got along well by simply being given a liquid diet as tolerated during the first twenty-four hours and the regular hospital diet thereafter. Since earlier ambulation has been practiced, nutrition and metabolic balance have become much less of a problem requiring parenteral therapy.

Other Postoperative Medication.—Constant vigilance was observed against the excessive use of narcotics; no routine narcotic orders were allowed. The use of cathartics was avoided. Reliance on beta-hypophamine and neostigmine for the treatment of distention was gradually abandoned in favor of suction.

Suction and Ambulation.—Two aids of a mechanical nature have been of great help in furthering good results. One of these is the continuous aspiration of gastric, duodenal or intestinal contents through a Levin tube according to the method of Wangensteen or by means of the longer Miller-Abbott tube. Although suction was needed in only 100 of the 1,411 cases, the need in those cases for prompt prevention

or relief of distention was vital, and in more than one instance this procedure may well have been a lifesaving measure.

The other aid of a mechanical nature has been early ambulation. Although difficult to assess as a lifesaving measure, its increasing use has lessened morbidity in an interesting and surprising manner. In the entire ten year period only 11 per cent of the patients were allowed up on the first postoperative day, 17.5 per cent by the third day and 65.5 per cent by the seventh day. In 1947, 66 per cent got up on the first day, 86.5 per cent by the third day and 97 per cent by the seventh day. Early ambulation has not only gotten patients up more promptly but has correspondingly reduced the number of days in the hospital after operation. Over the entire period, 40 per cent of the patients were discharged from the hospital in seven days or less after the operation and 83 per cent by the fourteenth day. For the year 1947, the figures were 68 per cent and 90 per cent respectively.

SUMMARY

In a search for factors contributing to a zero mortality rate of acute appendicitis for the last five and one-half years, we have reviewed the 1,411 cases of that disease encountered in our clinic during the past ten years. Data regarding the clinical material, the type of operation used, postoperative care, complications and mortality have been presented and analyzed.

CONCLUSIONS

As a result of this analysis we conclude that in spite of the indisputable help of the sulfonamide and antibiotic drugs the prime factors in the elimination of mortality in acute appendicitis are (1) the alertness with which symptoms and signs of the disease are recognized, (2) the promptness with which the patient is brought to operation after diagnosis and (3) the consistent use of an operative technic which is sound in conception and safe in detail for the difficult as well as for the uncomplicated case.

ABSTRACT OF DISCUSSION

DR. FREDERICK F. BOYCE, New Orleans: Dr. McGraw's incredibly good results contrast with the statistics for acute appendicitis for a recent sixteen year period at the New Orleans Charity Hospital, where, by an erratic but generally progressive decline, the mortality has now fallen to approximately 3 per cent. Rupture continues to take a high toll and abscess is clearly not the desirable eventuality certain communications in the recent literature might suggest.

I question Dr. McGraw's contention that surgical treatment may safely be postponed for a walled-off abscess. An unruptured, appendix wrapped in omentum sometimes masquerades under that guise. Moreover, a walled-off abscess may rupture intraperitoneally. There were 4 deaths from that accident in the Charity Hospital series.

I also question Dr. McGraw's emphasis on the McBurney incision as an important factor in his excellent results. My own feeling is that details of

technic have little influence on the mortality. At the New Orleans Charity Hospital the lowest mortality was with the transverse incision. With this exception, incisions other than the McBurney were used chiefly in delayed, complicated and diagnostically difficult cases, groups in which the mortality would naturally be higher. The mortality of the various surgical procedures was, as always, an index of the severity of the pathologic process, not of the value of the operation.

For several reasons, the mortality at the New Orleans Charity Hospital is higher than at the Henry Ford Hospital. Our patients are all indigent and often ignorant. Negroes, who accounted for only 28 per cent of the cases of acute appendicitis, accounted for 42 per cent of the deaths. The mortality in the upper age brackets is still appallingly high. Most important of all, even in recent years more than half of all patients were not seen until twenty-four hours or more after the onset of illness. These considerations explain why 1 in every 4 appendixes was ruptured at Charity Hospital, against 1 in every 16 at the Henry Ford Hospital.

The present Reginald Fitz suggested that contributions on acute appendicitis, such as his father's original contribution, be read before medical, not surgical, groups, since the physician, not the surgeon, usually sees the patient first and thus controls his surgical destiny. The great John B. Murphy is said to have devoted part of every day to denouncing delay in the diagnosis and treatment of this disease. The universal application of those two concepts would go far toward solving the problem of acute appendicitis.

Dr. M. M. Zinninger, Cincinnati: I wish to congratulate Dr. McGraw on the excellent results that he and his associates at the Henry Ford Hospital achieved in the treatment of acute appendicitis. These results could have been attained only by the careful application of sound, fundamental surgical principles. Of these I should like to point out three which I believe are most important: (1) prompt operation as soon as the diagnosis of appendicitis is made, unless the condition of the patient precludes immediate operation; (2) the use of the McBurney incision, and (3) inversion of the appendical stump. My preference is for inhalation anesthesia, but in the Cincinnati General Hospital series in which a fair proportion of the patients operated on were under spinal anesthesia, there is no evidence that the morbidity or mortality was significantly altered by either type of agent.

While our mortality statistics are much higher than Dr. McGraw's, it should be remembered that they come from a large municipal charity hospital and not a private hospital. The mortality rate has been progressively lowered, and I should like to give you an explanation for the reduction. The first period, from 1915 to 1922, was before the establishment of a resident training system; often there was some delay in getting a staff surgeon to see or operate on a patient. In addition, the right rectus was the incision of choice during those years. With the development of a resident training system, prompt operation through a McBurney incision became the routine procedure. This, I believe, explains the drop in mortality from 9.5 to 5.4 per cent for the periods 1915 to 1921 and 1922 to 1933, respectively.

From 1922 until the present, the operative principles employed have not changed significantly and are essentially the same as those Dr. McGraw described, so that other explanations for the lowered mortality rate must be found. One of the most important, I believe, was education of the people of Cincinnati to come to the hospital earlier for the treatment of appendicitis. For example, for the period 1915 to 1933, the average elapsed time from onset of symptoms till the patient reached the hospital was approximately ninety-one hours (nearly four

days), and 42.5 per cent of the patients had perforation of the appendix when they reached the hospital. In the next five year period, the average elapsed time decreased from ninety-one to fifty-eight hours and the incidence of perforation from 42.5 to 36 per cent. In the period 1939 to 1943, a further drop to fifty-four hours elapsed time and to 30 per cent perforations occurred. This change was brought about by an intensive educational campaign carried out by the Public Health Federation and the Academy of Medicine, and was observed in all Cincinnati hospitals.

Significant improvements in management also occurred during these years and, in my opinion, the most important in reducing mortality were (1) the introduction of continuous gastric suction by Wangensteen's method in the middle thirties, (2) improvements in anesthetic methods and use of new anesthetic agents and (3) increased use of blood transfusion and other parenterally administered supportive therapy, before and after operation.

The second slide shows a rather striking reduction in mortality which I believe can be accounted for only by the introduction of chemotherapeutic and antibiotic agents, principally penicillin and, more recently, streptomycin. While sulfanilamide compounds caused some change, the striking reduction seems to have come in 1945 when penicillin first became freely available.

DR. J. L. CROOK, Jackson, Tenn.: In my presidential address delivered before the Southern Medical Association at Hot Springs, Ark., twenty-seven years ago, I said that I believed the highest type of service which the medical profession can render to the public is education of the public.

In my section of the country operations that were done late were almost the only ones in which mortality resulted. My first appendectomy outside of a hospital was performed fifty years ago. It took me all day to get to the place where I was to operate, which was 40 miles from the railroad on the banks of the Tennessee River. My operating table was three planks from the barnyard laid on a kitchen table and a barrel. That patient got well, and I saw him thirty years afterward in Jackson. He recognized me and introduced himself.

The point I wish to make is that the use of purgatives and delay in operation are the two factors responsible for mortality. It is on these two points that education is sorely needed, for both delay and the use of purgatives are due to ignorance. If the public could only be educated to the fact that appendicitis is primarily and entirely a surgical disease and that the patients' lives depend on prompt appearance at a good hospital with an able and conscientious surgeon in charge, mortality would be almost entirely eliminated.

DR. ARTHUR B. MCGRAW, Detroit: I wish to thank all three discussants for their remarks, and particularly for their emphasis on the importance of lay education. We at Henry Ford Hospital are quite aware of that need, though it was not possible in the limited time to deal with that factor.

There is another matter I should like to mention. I want to make it completely clear that the results here reported with regard to mortality in this disease do not in any sense represent solely a personal achievement. These results were possible because of consistent group effort by the entire staff of the division of general surgery, and of a rather large number of young resident surgeons.

UNFAVORABLE REACTIONS TO OXIDIZED CELLULOSE (OXYCEL) IN THE BED OF THE GALLBLADDER

The "Retained Oxycel Sponge Syndrome"

EDWARD S. VANDERHOOF, M.D.
AND
K. ALVIN MERENDINO, M.D.
MINNEAPOLIS

SINCE the early work on oxidized cellulose by Yackel and Kenyon [1] in 1941, repeated experiments have been conducted on laboratory animals in order to evaluate its hemostatic action, absorbability, and the reaction of tissues to it. Putnam [2] embedded small pieces of oxidized cellulose paper in the abdominal muscles of cats and dogs and demonstrated the complete absorption of the material in most cases. He also implanted pieces of oxidized cellulose gauze in the folds of the omentum in dogs. Examination after eleven days revealed a thickening of the omentum, but microscopic study demonstrated a minimal inflammatory reaction and the complete resolution of the gauze. Uihlein and others [3] conducted studies which indicated that a complete dissolution of the oxidized gauze occurred in four and a half days when it was placed in human surgical wounds. Oxidized cellulose was packed into experimentally produced lacerations of dog's liver, kidney and spleen by Frantz.[4] In each instance the bleeding was satisfactorily controlled.

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Dr. Merendino, on Jan. 1, 1949, assumed the duties of Associate Professor of Surgery, University of Washington, Seattle.

From the Department of Surgery, University of Minnesota, Minneapolis, and the Surgical Service of the Ancker Hospital, St. Paul, Minn.

1. Yackel, E. C., and Kenyon, W. O.: Oxidization of Cellulose by Nitrogen Dioxide, J. Am. Chem. Soc. **64**:121-127 (Jan.) 1942.

2. Putnam, T. J.: The Use of Thrombin on Soluble Cellulose in Neurosurgery: Preliminary Note, Ann. Surg. **118**:127-129 (July) 1943.

3. Uihlein, A.; Clagett, O. T., and Osterberg, A. E.: The Use of Oxidized Cellulose for Hemostasis in Surgical Procedures: Preliminary Report, Proc. Staff Meet., Mayo Clin. **20**:29-32 (Jan. 24) 1945. Uihlein, A.; Clagett, O. T.; Osterberg, A. E., and Bennett, W. A.: Absorbable Oxidized Cellulose with Thrombin as a Hemostatic Agent in Surgical Procedures, Surg., Gynec. & Obst. **80**:470-472 (May) 1945.

4. Frantz, V. K.: Absorbable Cotton, Paper, and Gauze (Oxidized Cellulose), Ann. Surg. **118**:116-126 (July) 1943.

The early clinical use of oxidized cellulose as a hemostatic agent was made in neurosurgery. In some cases thrombin was used in conjunction with oxidized cellulose.[2] However, it was discovered early that the acid reaction of the oxidized cellulose inactivated the thrombin. Neutralization of the carboxyl groups of the cellulose by proper amounts of sodium bicarbonate eliminated the inactivation. Frantz [5] reported 3 cases in which this material had been used in the control of bleeding from the bed of the gallbladder following cholecystectomy. In the first case drainage was carried out. Healing occurred on the fourteenth postoperative day. In case 2 a biliary fistula persisted from the second to the seventeenth postoperative day. Some bleeding was observed on the ninth postoperative day. The patient in case 3 had an uneventful convalescence.

In view of our own difficulty in 3 of 4 cases in which a single "oxycel" sponge had been left as a permanent hemostatic agent in the bed of the gallbladder after cholecystectomy, we feel that these cases should be recorded, with a word of warning.

PRESENTATION OF CASES AND COMMENT

CASE 1.—C. H., a 29 year old Negro woman, was admitted to the Ancker hospital on June 23, 1947, and readmitted on July 14. She was discharged on July 10, 1947, after the first admission and on August 9, after the second admission.

The patient gave a history of intermittent pain in the right upper quadrant of four years' duration related to the ingestion of fatty foods, cabbage and beer.

A cholecystogram revealed a nonfunctioning gallbladder. A single rounded density was seen in the area of the fundus of the gallbladder, which was thought to represent a stone. A series of gastrointestinal roentgenograms was normal.

On July 2, 1947, a routine cholecystectomy was performed. A large solitary stone was found in the lumen of the gallbladder. After the removal of the gallbladder, a single "oxycel" sponge was placed in the gallbladder bed. A Penrose drain was placed down to the amputated stump of the cystic duct and brought out through a stab wound lateral to the incision. Immediately after operation there was a rise in the patient's temperature to 101.4 F. By the second postoperative day, however, the temperature had returned to normal. The patient was discharged from the hospital on her eighth postoperative day completely ambulatory.

The pathologic report described the presence of chronic cholecystitis and cholelithiasis.

The drain was removed partially on the day before discharge, and by the twelfth postoperative day it was completely out.

Four days after her discharge the patient was readmitted to the hospital complaining of pain in the right upper quadrant and in the back, vomiting and weakness. The temperature was 101.4 F., and the leukocyte count was 11,800, with 86 per cent polymorphonuclear cells. A large area of induration developed on the patient's right side, extending from the costal margin to the iliac crest. A subcutaneous infection was suspected. Therefore, a small incision was made lateral to the

5. Frantz, V. K.; Clarke, H. T., and Lattes, R.: Hemostasis and Absorbable Gauze, Ann. Surg. **120**:181-199 (Aug.) 1944.

original incision. No pus was encountered. Subsequently, a fluoroscopic examination demonstrated both diaphragms to be moving well with respirations. A small amount of fluid in the right side of the chest obliterated the costophrenic angle. A flat plate roentgenogram of the abdomen revealed loculated small pockets of air in the subhepatic space.

On July 28 the patient's abdomen was reexplored. In view of the presence of fluid in the right side of the chest, the right subdiaphragmatic suprahepatic space was explored extraperitoneally. It was found to be normal. The incision through the Clairmont approach was closed and a separate incision made over the subhepatic area. A large abscess was encountered and drained. Approximately 400 cc. of chocolate-colored pus were obtained. Fragments of "oxycel" and of necrotic tissue were seen in the material from the abscess. The drains were removed by the eleventh day. The patient was discharged with all wounds healed and has remained well.

Bacteriologic studies of the material from the subhepatic abscess revealed nonhemolytic streptococci, nonhemolytic staphylococci and gram-positive cocci in pairs.

CASE 2.—Mrs. A. M. W., a 25 year old white woman, was admitted to the Ancker hospital on Dec. 6, 1946, and readmitted on Dec. 23, 1946. She was

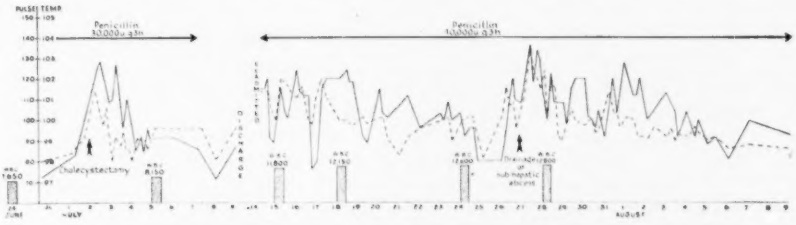

Fig. 1 (case 1).—The cholecystectomy was performed with ease. There was no spillage at the time of operation. The pathologist's diagnosis was chronic cholecystitis with stones. Shortly after the patient's discharge from the hospital there was a recurrence of pain in the right upper quadrant, sufficiently severe to necessitate rehospitalization. After drainage of a subhepatic abscess, the patient progressed to complete recovery.

discharged on December 19, 1946, after the first admission and on December 30 after the second admission.

The history revealed that the patient had suffered from repeated gallbladder attacks since 1944. These attacks were characterized by epigastric pain following the ingestion of fatty foods. One week previous to her admission, she noted clay-colored stools and dark urine. However, no jaundice was evident on her entry to the hospital.

Cholecystogram revealed a nonfunctioning gallbladder. A series of gastrointestinal roentgenograms was normal.

On Dec. 13, 1946, an exploratory laparotomy was performed. The wall of the gallbladder was thickened slightly, and numerous stones could be easily palpated. A cholecystectomy was performed in a retrograde fashion, without event. One "oxycel" sponge was sutured into the bed of the gallbladder by means of surgical gut. A single Penrose drain was laid down to the site of the amputated cystic stump and was brought out through a stab wound in the right upper quadrant.

The immediate postoperative course was uneventful, and the patient was discharged, ambulatory, on her sixth postoperative day.

The pathologic report described the presence of acute and chronic cholecystitis, and cholelithiasis.

The gradual removal of the Penrose drain was begun in the outpatient department on the seventh postoperative day and was completed on Dec. 23, 1946.

Four days after her discharge the patient was readmitted with fever and with severe pain in the right upper quadrant. There was resistance to palpation in this area, as well as tenderness and rebound tenderness. Roentgenograms of the chest showed no evidence of pneumonitis. Examination of the urine revealed it to be normal. With penicillin therapy and rest in bed the temperature subsided and the pain gradually disappeared. The patient was discharged one week after her second admission. She has remained symptom free.

CASE 3.—Mrs. O. L. P., a 67 year old white woman, was admitted to the hospital on Feb. 18, 1947, and discharged on April 4. She was admitted initially to the medical service with cardiac failure. Digitalization controlled this difficulty in a satisfactory manner. While on the medical service a series of gastrointestinal roentgenograms and a gastroscopic examination revealed a gastric

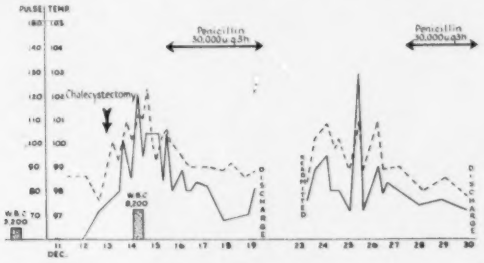

Fig. 2 (case 2).—After an uneventful cholecystectomy, the patient was discharged, ambulatory, on the sixth postoperative day. Four days after her discharge she was readmitted with symptoms similar to those which she experienced during her previous gallbladder attacks. The physical signs present suggested an acute inflammatory process in the right upper quadrant. It is possible that the use of penicillin averted the development of a surgical abscess.

ulcer on the lesser curvature of the stomach, which was considered to be malignant. Numerous radiopaque stones could be seen in the region of the gallbladder at the time of the gastrointestinal examination.

On March 15, 1947, exploration was carried out through a subcostal incision on the left side. An area of induration was found on the lesser curvature of the stomach at the incisura angularis. Consequently, resection of 75 per cent of the stomach was carried out. The gallbladder, which appeared to be normal except for the evidence of numerous stones on palpation, was removed in a retrograde fashion, without event. One "oxycel" sponge was left in situ. The area was drained with a single Penrose drain, which was brought out through a separate stab wound.

The pathologic report described the presence of chronic cholecystitis, cholelithiasis and benign gastric ulcer.

The postoperative course was uneventful until the seventh postoperative day, when the temperature rose to 101.4 F. It subsided in three days after the Penrose

drain began to draw off copious quantities of a yellowish fluid, which was not bile. This drainage persisted for but a few days, and the wound then healed completely after the gradual removal of the drain. There have been no subsequent symptoms referable to the operation.

It is interesting that in the initial case (case 2) the patient was symptomless and afebrile at the time of her discharge following the cholecystectomy. On her readmission to the hospital, however, her complaints were similar in most respects to those which she related at the time of her first admission, but they were of greater severity. With conservative management and the administration of penicillin,

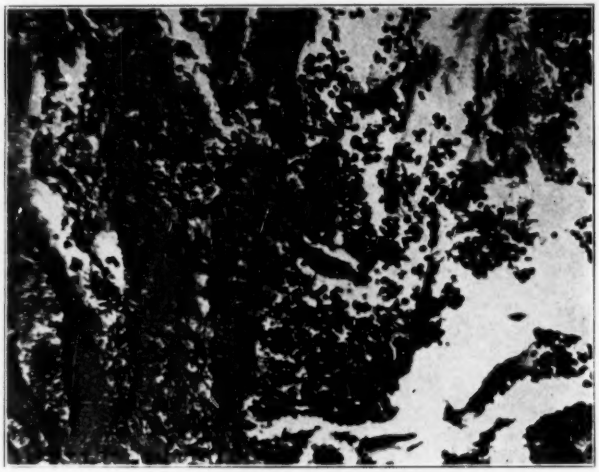

Fig. 3.—Sections of the material from the abscess show it to be composed of acute inflammatory cells together with masses of pink-staining homogenous foreign material, the character of which cannot be determined from the microscopic examination. There is no evidence of foreign body giant cells. The diagnosis was foreign material in an abscess cavity (Dr. John F. Noble). This pink-staining homogenous material undoubtedly represents fragments of the "oxycel" sponge identified on gross examination.

the symptoms and signs gradually abated (fig. 2). It was felt at this time that the patient's difficulty was directly related to the implanted "oxycel" sponge. Consequently, it was decided to treat additional patients in a similar fashion in order to evaluate this impression more accurately. Case 3 involves a patient in whom the cholecystectomy was incidental to a more serious operative procedure. The gallbladder was undoubtedly quiescent. Although a gastric resection was performed at the same time, an aseptic closed anastamosis was carried

out, without contamination. The lesion was a gastric ulcer, and consequently the duodenal stump was inverted aseptically, without event. The rise in the temperature on the seventh postoperative day, followed by a profuse serous drainage, suggested a reaction of the tissue adjacent to the "oxycel" sponge.

In case 1 the severest complication was encountered. The similarity of the sequence of events between this case and case 2 is striking, viz., an uncomplicated immediate postoperative convalescence followed by discharge from the hospital and then a short interval of quiescence, with the subsequent recurrence of pain in the right upper quadrant. Both patients required rehospitalization (fig. 1). There was some delay in establishing the correct diagnosis at the time of the second admission of the patient in case 1. However, the correct diagnosis was made preoperatively. The presence of fluid in the right side of the chest suggested the possibility of a concomitant subdiaphragmatic infection. This was considered unlikely. Nevertheless, the right subdiaphragmatic suprahepatic space was explored first in order to insure a clean operative site. After this area was found to be normal, as anticipated, the incision was closed. A separate incision was made then over the subhepatic area. A markedly indurated mass was palpated and ruptured. The fragments, some rather large, of the "oxycel" sponge together with pieces of necrotic tissue were found in the abscess. Undoubtedly, the sponge represented the nidus for the infection itself (fig. 3). It is unlikely that the sponge was contaminated prior to its insertion.

In the 3 cases in which unfavorable reactions have been encountered the signs and symptoms have become manifest between the seventh and the twelfth postoperative day. The patients have presented a characteristic picture. The symptoms and signs have been more severe than one encounters with some of the ordinary complications following cholecystectomy. Pain has been an outstanding feature of this clinical picture. In fact, the house staff had become so sensitized to the sequence of events that the last patient (case 1) was admitted to the hospital with the diagnosis of "possible retained oxycel sponge syndrome."

SUMMARY

The pertinent literature on oxidized cellulose, "oxycel," has been reviewed. Only 3 cases have been recorded in the literature in which oxidized cellulose has been implanted in the bed of the gallbladder and left in situ. No unfavorable reaction was noted which could be attributed to the effect of this material. We have treated 4 patients in this fashion, 3 of whom reacted unfavorably. The most severe

complication was the development of a subhepatic abscess, which necessitated surgical drainage. Because of this experience with oxidized cellulose left in situ as a means of controlling the bleeding from the bed of the gallbladder, we feel that the material should not be used as a "permanent" hemostatic agent for such a purpose. Furthermore, one should thoughtfully consider the wisdom of similarly implanting this material anywhere in the abdominal or thoracic cavity.

PROGRESS IN ORTHOPEDIC SURGERY FOR 1946

A Review Prepared by an Editorial Board of the American Academy of Orthopaedic Surgeons

IX. INFECTIONS OF THE BONES AND JOINTS

Prepared by
PHILIP LEWIN, M.D., CHICAGO

Silly Names for Penicillin Products.—In February 1946 The Journal of the American Medical Association[361] called attention editorially to a great variety of names for penicillin that had been introduced by manufacturers and purveyors. So many names had been offered that they seemed designed to conceal rather than reveal the nature of the product. Now come other titles that fail to indicate the nature of the product but which suggest the section of the body, or the animal, at which they are aimed, or that are otherwise as ridiculous. Here are a few samples from recent lists:

Buffecillin (Pfizer)
Crysticillin (Squibb)
Dairycillin (Schenley)
Duracillin (Lilly)
Flo-Cillin (Bristol Laboratories)
Gelu-Cillin (Warner)
Hypercillin (Cutter)
Intracillin (Warner)
Par-Pen (Smith, Kline & French)
Pecticillin (Kline)
Pelvicin (Schenley)
Pen-Troche (Cutter)
P. O. B. (Cutter)
Poultrycillin (Schenley)
Powdalator (Abbott)
Wycillin (Wyeth)
Capicillin (Barron Chemical Corp.)
Denticillin (Marlo Laboratories)
Nasocillin (Mo-La Laboratories)
Ophtocillin (Marlo Laboratories)
Rectocillin (Mo-La Laboratories)
Salvacillin (Barron Chemical Corp.)
Tablicillin (Barron Chemical Corp.)
Trochicillin (Marlo Laboratories)
Vagicillin (Marlo Laboratories)

To select a rose from such a garden would require a botanist with more basic knowledge of the naming of plants than most physicians possess. Perhaps the blue ribbon should go to either "Poultrycillin" or "Vagicillin." Perhaps the next step will be numbers to correspond with certain entrances or exits of the human body; we may be talking about "cillin no. 1" for the front and "cillin no. 2" for the rear. In a previous editorial, attention was called to the combination of the manufacturer's name with "cillin." Since there were almost thirty manufacturers, that offered almost thirty possibilities. Now the emphasis seems to be inclining toward the port of entry plus "cillin."

The Clinical Diagnosis, Prognosis and Treatment of Acute Hematogenous Osteomyelitis.[362]—There is a definite trend against early

361. More Silly Names for Penicillin Products, editorial, J. A. M. A. **137:** 1043 (July 17) 1948.

362. Dickson, F. D.: The Clinical Diagnosis, Prognosis and Treatment of Acute Hematogenous Osteomyelitis, J. A. M. A. **127:**212-217 (Jan. 27) 1945.

drainage of the localized bone abscess in hematogenous osteomyelitis. The bacteriostatic effects which the sulfonamide drugs exert seem unquestionably to bring about the disappearance of the constitutional symptoms and control the local bone infection in some cases. These drugs, however, can have no effect on the local bone destruction which has occurred before the infection was brought under control, and the necrotic tissue which results remains as a possibly quiescent unhealed focus in the bone. As long as the roentgen rays reveal definite areas of bone destruction and sequestrum formation, no matter how silent the area may be clinically, the condition cannot be spoken of as cured but only as one which shows a clinical recession with a quiescent bone focus. Such quiescent areas may remain dormant for years and in some cases permanently. However, an examination of a number of patients treated by the administration of the sulfonamides without drainage has shown that in practically all a careful roentgenologic examination revealed persistent areas of bone destruction which are readily differentiated from the surrounding normal bone. Such areas constitute potential sources of trouble in the future. Wilson and McKeever report on 3 patients treated by administration of the sulfonamides without drainage, with subsidence of acute symptoms, for whom several months later drainage was established because of persistent local induration. Thick, soft, hyperplastic bone was encountered, and granulation tissue was found in the medullary canal when drainage was established. Smears and cultures revealed staphylococci. These findings clearly indicate that such quiescent foci harbor dormant bacteria capable of activity.

Treating a bone abscess with sulfonamide drugs and without drainage may result in putting out the fire; but the ashes remain, and only too frequently ashes which have embers likely to be fanned into activity by such breezes as lowered resistance or local trauma to the quiescent area. Dickson's observations have convinced him that sooner or later a large percentage of these quiescent foci become active. Whether penicillin proves to be an agent which, more powerful than the sulfonamide drugs, will completely sterilize such areas of infection only time will tell. Until then the preponderance of evidence is in favor of early drainage of the osseous focus in acute hematogenous osteomyelitis except in the fulminating type with septicemia and pyemia, in which the drainage of a single focus, when there are probably others present, cannot be expected to have any helpful effect but will probably do harm.

Chronic Sclerosing Osteomyelitis.—The patients included in Meyerding's [363] series of 80 cases had an average age of 25 years, appeared to be in good health and were not disabled. The preoperative clinical laboratory findings in the blood and urine were of little value in the diagnosis. Trauma may have been an inciting factor in 31.2 per cent of the cases.

The outstanding symptom was persistent localized pain in 93.8 per cent of cases. In 67.5 per cent of cases this was associated with swelling. The duration of symptoms averaged 1.4 years. Sixty-five per cent of the patients were males. In 92.5 per cent of cases the lesions were located in the lower extremity; 50 per cent occurred in the middle third of the shaft of the long bones, and 90 per cent occurred in the shaft of the tibia or femur. Patients aged from 10 to 30 years comprised 69 per cent.

The roentgenograms revealed dense spindle-shaped cortical regions of sclerosis that involved the shaft of the long bones. Translucent regions, small and round or oval, were often visible. These regions sometimes showed staphylococci on bacteriologic examination of material removed at operation and have been looked on as foci of infection producing the sclerosis.

The treatment recommended is surgical incision, and the results obtained are good.

Treatment of Acute Staphylococcic Osteomyelitis With Penicillin and Without Surgical Operation.—Penicillin therapy without any early surgical procedure was employed in 8 cases of acute hematogeneous osteomyelitis, in 6 of which a demonstrable bacteremia was present.[364] There were no deaths. Except in 1 case, in which the authors believe treatment was inadequate, the results were uniformly good. Pain, fever and swelling were diminished within a day or two, and steady improvement usually followed.

Roentgenographically, visible changes, with rarefaction and periostitis, occurred in most of the cases regardless of penicillin therapy, but as a rule these lesions healed in a few months. The patients for the most part were clinically well within one to two months. Intensive penicillin treatment over several weeks is advocated by the authors for acute osteomyelitis.

The reporting of these cases is not to be understood as a final recommendation that in every instance of acute osteomyelitis, treatment without operation should be employed. Even if penicillin is given,

363. Meyerding, H. W.: Chronic Sclerosing Osteomyelitis, Tr. West. S. A. **52**:545-564, 1944.

364. Bloomfield, A. L.; Kirby, W. M. M., and Armstrong, C. D.: Treatment of Acute Staphylococcic Osteomyelitis With Penicillin and Without Surgical Operation, Stanford M. Bull. **3**:161-175 (Nov.) 1945.

the physician must use his judgment as to the advisability of surgical intervention as well.

Salmonella Osteomyelitis.—Three cases of salmonella infection of bone are reported.[365] In all of these a salmonella organism was originally obtained in pure culture, either from the bone focus or from a local abscess, and all subsequent cultures of the wounds revealed only secondary invaders and not the original causative organism. It is possible, therefore, that many atypical cases of chronic osteomyelitis or solitary bone abscesses may be due to salmonella infection. The salmonella organism may be subsequently overgrown by the secondary bacterial invaders, which mask the original causative organism. Cultures of the bone focus at operation or of pus aspirated from a local abscess should be made in every case to determine the initial pathogen.

All of these cases showed a similar clinical picture. There is usually a mild systemic reaction or none. There are only minimal evidences of local inflammation despite the formation of soft tissue abscesses. The bone focus is chronic, and the symptoms may be so mild that they cause little discomfort even over a long period and the lesion may lie dormant for many years. Roentgenograms show a characteristic picture consisting of a well defined rarefaction shadow, with essentially no reaction of the surrounding bone. There is no medullary sclerosis, cortical thickening, periostitis or sequestration, as usually seen in staphylococcic osteomyelitis. There is likewise no atrophy of osseous or soft tissues surrounding the lesion, as is commonly seen in tuberculosis of bone.

Penicillin and sulfadiazine were given, with no demonstrable effect although the therapy was not pushed vigorously. At the time the patients were treated, streptomycin was not available for trial. It appears that primary closure of the wound after operation is not advisable as it usually leads to sinus formation. Saucerization with healing from below was successful in 1 case, whereas cleaning out the local abscess was sufficient in the third case. It is difficult to be sure whether any of the patients are permanently cured, particularly in view of the dormant tendency so characteristic of this condition.

Pneumococcic Arthritis Treated With Penicillin.—Six cases of pneumococcic arthritis due to types I, V, VIII, XII and XXVIII are reported.[366] Penicillin was administered intravenously and intramuscularly in 5 patients, 3 of whom also received it intra-articularly.

365. Seidenstein, H.: Salmonella Osteomyelitis, Bull. Hosp. Joint Dis. **6**: 126-132 (Oct.) 1945.

366. Bunim, J. J.: Pneumococcic Arthritis Treated with Penicillin: Report of Six Cases, M. Clin. North America **30**:584-596 (May) 1946.

Prompt sterilization of the blood stream and subsequent sterilization of the synovial fluid followed. Surgical treatment was not necessary in any instance.

Prognosis as to life is governed not by the arthritis but by the severity of the associated extra-articular infection. Two patients died; 1 died of bacterial endocarditis and the other was in a moribund state fifty-eight hours after admission to the hospital.

The Use of Penicillin in the Treatment of Acute Hematogenous Osteomyelitis in Children.—Twelve cases of acute hematogenous osteomyelitis,[367] in children aged 3 to 12 years, have been studied. Penicillin was employed successfully in the treatment of each of the 12 patients. The infection in 10 of the patients treated successfully by penicillin had proved to be resistant to the sulfonamide drugs. Surgical treatment was necessary in 4 of the 12 patients—in 1 for the removal of a small sequestrum and in 3 for the drainage of an abscess after the acute infection had subsided.

Penicillin appears to be a more effective agent in the treatment of acute hematogenous osteomyelitis than any other therapeutic agent. Early use in adequate doses administered at frequent intervals may not only cure the initial infection but may prevent spread to other bones and in a majority of cases may make surgical intervention unnecessary.

If use of penicillin is not started until after a bone has been extensively damaged, with necrosis of segments of cortex, central destruction of bone and cavity formation, late surgical treatment may become necessary.

From the authors' experience in this series of cases, they hazard the suggestion that in children aged 3 to 12 years, acute hematogenous osteomyelitis may be effectively treated if penicillin is administered intramuscularly in doses of 15,000 to 20,000 units each every three hours day and night. After the temperature begins to subside, the size of each dose may be reduced to 10,000 units, but the frequency of dosage must be maintained. When the patient becomes afebrile the dosage may be reduced gradually and discontinued after five days of normal temperature. Recurrences may occur if penicillin is stopped too soon.

While making use of a remarkable chemotherapeutic agent such as penicillin, one must not neglect to use well established principles of medical care, such as the maintenance of the fluid balance of the body through the administration of isotonic sodium chloride solution, glucose, plasma or blood. Splints, plaster casts or traction should be used when they are needed for supporting the diseased bone or to prevent contractures.

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367. Compere, E. L.; Schnute, W. J., and Cattell, L. M.: The Use of Penicillin in Treatment of Acute Hematogenous Osteomyelitis in Children: Report of Twelve Consecutive Cases, Ann. Surg. **122**:954-962 (Dec.) 1945.

Acute Hematogenous Osteomyelitis Treated With Penicillin.—Thirty patients with acute osteomyelitis have been treated with penicillin in eighteen months.[368] Blood culture was positive in 14 cases. Penicillin was first given systemically in a dose of 100,000 units in twenty-four hours. On theoretic grounds this dose was increased in later cases to a maximum of 400,000 units to obtain a concentration which should be bactericidal as well as bacteriostatic. When the infection appeared to be adequately controlled, the dose was reduced to a minimum of 100,000 units in twenty-four hours.

Two well defined groups of patients were distinguished: (1) those admitted before the bone was seriously damaged and before pus had formed and (2) those admitted with an abscess already present.

Group 1 could be treated successfully by systemic administration of penicillin alone, provided the course was sufficiently long and intensive; the condition might resolve without any roentgenographic evidence of bone changes. Seven of 30 (1 in 4) patients admitted were suitable for this treatment. Group 2 must be treated surgically, as well as with penicillin, and surgical treatment must include release of pus in the bone by drilling; after this, primary suture is safe and advisable to prevent secondary infection.

Patients in group 2 not treated by operation as well as penicillin developed a spreading decalcification of the bone, the area of which increased over one to five months. Workers at other centers have confirmed this.

In this series there was no death, no joint involvement and no secondary focus after admission. At the end of eighteen months, 4 patients still have a sinus, but 2 of these are nearly healed; 28 have normal function, 1 admitted with septic arthritis of the knee has limited range of movement and 1 has a sinus which keeps her in the hospital.

The importance of surgical drainage in these cases is discussed.

One case of infection with a penicillin-resistant organism was encountered early in this series. It is not included in the series, because at the time the authors had not sufficient penicillin for its adequate treatment. The organism was four times as resistant as the normal staphylococcus; it would have required at least 400,000 units of penicillin in twenty-four hours for bacteriostasis. The case serves as a reminder that the sensitivity of the organism must always be tested.

Report on the Use of Penicillin in the Treatment of Staphylococcic Infections With Special Reference to Acute and Chronic Osteomyelitis and Several Collateral Studies.—This project has demonstrated the

368. Agerholm, M., and Truetta, J.: Acute Hæmatogenous Osteomyelitis Treated with Penicillin, Lancet **1**:877-881 (June 15) 1946.

manner in which penicillin is useful in the treatment of suppurative lesions in general and of osteomyelitis lesions in particular.[369] It has also made possible radical modifications in the treatment of acute and chronic osteomyelitis to the end that morbidities are greatly diminished and convalescence greatly shortened. Though the authors' experiences and follow-up periods have been all too short to reach final conclusions, they nevertheless have been sufficiently clear to make some of the following conclusions reasonably certain and some others only tentative.

"(1) To be effective penicillin must be brought in intimate contact and in sufficient concentration with the offending micro-organism whether it be in the blood stream or in some localized focus. Localized foci when fully developed are usually not influenced by the systemic administration of the antibiotic, unless they are brought into close communication with the blood stream. The local application of penicillin is essential to the treatment of localized foci.

"(2) In acute hematogenous osteomyelitis, early local lesions which are not fully developed may be aborted, and small local lesions may be made to retrogress by the use of the systemic administration of penicillin. Large, fully developed foci are not influenced and though the surgical approach is made nonurgent, it is nevertheless necessary before the focus can be eradicated. The bacteremia is controlled and the metastasizing of the focus can probably be prevented by systemic therapy if the organism is susceptible.

"(3) In chronic osteomyelitis, the use of pre- and post-operative administration of intramuscular penicillin and the local application of the drug prior to the closure of the wound without drainage has made possible the healing of extensively saucerized areas by primary intention. The immediate results are spectacular and the follow up of these cases has been most encouraging.

"(4) In acute suppurative arthritis and bursitis the intramuscular and the intraarticular or intrabursal use of penicillin has in our limited number of cases completely resolved the lesions.

"(5) In acute suppurative soft tissue lesions healing by primary intention can in all probability be obtained, by incision and evacuation of the lesion, the local application of penicillin and primary closure of the wound in conjunction with the pre- and post-operative administration of penicillin systemically. In chronic lesions the fibrosed

369. Buchman, J., and Blair, J. E.: Report on Use of Penicillin in Treatment of Staphylococcal Infections with Special Reference to Acute and Chronic Osteomyelitis and Several Collateral Studies, Bull. Hosp. Joint Dis. **6**:114-125 (Oct.) 1945.

abscess wall or sinus tract must be excised before healing by primary intention can be obtained.

"(6) The use of penicillin in acute postoperative bone and joint infections has been totally ineffective in their experience. Thorough drainage and complete removal of devitalized tissue and foreign bodies are essential before healing can be induced.

"(7) Tuberculous bone and joint lesions with secondary infections can be subjected to operative procedures and primary healing of the wound can be obtained by the thorough removal of the disease focus, the obliteration of the adjacent sinus tracts and the local application of penicillin prior to the closure of the wound without drainage in conjunction with the systemic administration of penicillin during the pre- and post-operative periods. A fair proportion of their limited number of cases have yielded good results. This method is worthy of further trial.

"(8) Healing by primary intention can be obtained in surgical procedures in close proximity to suppurative lesions by the application of penicillin to the operative site prior to the closure of the wound without drainage in conjunction with the pre- and post-operative intramuscular administration of penicillin. This approach has in their experience made possible several one stage amputations with the preservation of the adjacent joints which under other circumstances would have had to be sacrificed.

"(9) They have had very satisfactory experiences with the administration of intramuscular penicillin during the pre- and post-operative periods and the local application of the drug before closure of the wound without drainage in extensive surgical procedures on patients with inactive osteomyelitic lesions.

"(10) The postoperative systemic administration of penicillin has apparently prevented imminent post-operative infections in instances in which the operative site had been contaminated or unduly traumatized.

"(11) A large proportion (78.5% in this series) of cultures of coagulase reaction is unaffected. This *in vitro* resistance is temporary; strains of definitely high natural resistance may be encountered.

"(12) Staphylococci may be made resistant to penicillin by growth in progressively increasing concentrations in broth. Their metabolic activity is retarded and their pathogenicity is reduced or lost. The coagulase reaction is unaffected. This *in vitro* resistance is temporary; restoration to sensitivity, but only partial return to pathogenicity, may be effected by serial transfer in broth.

"(13) Staphylococci may acquire resistance during penicillin therapy. This occurred in 21.9% of the cases in this series. The metabolic

activity of resistant strains is retarded, but their pathogenicity is often unaltered. Such strains produce an inhibitor of penicillin. The coagulase reaction is unaffected. This resistance which is developed *in vivo* appears to be permanent.

"(14) Penicillin has no effect on the development of the coagulase reaction. It occurs even in the presence of concentrations of penicillin which are ultimately bactericidal. Penicillin has no effect on the formation of staphylococcal alpha-toxin, and neither enhances or destroys preformed toxin.

"(15) It is suggested that some significance must be attached to the development of resistance by staphylococci during penicillin therapy, because of the tendency toward permanence of the resistance developed, the continued pathogenicity of such resistant strains, and their production of a substance which inhibits penicillin."

The Action of Penicillin on Staphylococci.—The resistance to penicillin which staphylococci may acquire during penicillin therapy tends to be permanent.[370] As a rule it is accompanied with little loss of pathogenicity. This is in contrast to the loss of pathogenicity by cocci which are made resistant in vitro, a fact which has been cited as a reason for attributing little clinical significance to resistance. It is of particular significance that the coagulase reaction of staphylococci, which is a reliable indicator of their potential pathogenicity, is not lost when they become resistant to penicillin. This suggests that the capacity for pathogenicity persists even when the cocci become resistant. This masked or latent pathogenicity of strains which are made resistant in vitro is restored on their restoration to sensitivity. The pathogenicity of strains acquiring resistance during penicillin therapy often persists unaltered. Penicillin per se has no effect on staphylococcic toxin. Therefore the possibility must be kept in mind that staphylococci which become resistant to penicillin during treatment may maintain the infection or may initiate new infection. In addition, these penicillin-resistant strains have been shown to be resistant to the bactericidal action of whole blood and to produce a potent inhibitor of penicillin.

The development of resistance to penicillin has been considered by some not to be a major factor in the treatment of staphylococcic infections. However, several instances have been reported of the acquisition of resistance by staphylococci during penicillin therapy. In some of these it appeared probable that resistance to penicillin was a factor contributing to clinical failure or to an occasional relapse or recurrence after apparent cure. For the reasons given, the authors feel that some significance must be attached to the development of resistance by

370. Blair, J. E.; Carr, M., and Buchman, J.: The Action of Penicillin on Staphylococci, J. Immunol. **52**:281-292 (March) 1946.

staphylococci during penicillin therapy. The isolation of penicillin-resistant staphylococci from patients as long as a year after discontinuance of therapy emphasizes this point.

Since inadequate dosage of penicillin has been considered to contribute to the development of resistance, the necessity for early intensive administration of penicillin in staphylococcic infections is obvious. Even this does not guarantee that any given staphylococcus will not become resistant. Individual problems of dosage may occur in infections due to naturally resistant organisms. In order for penicillin to be effective it is essential that intimate contact with the bacteria should occur. In infections such as chronic osteomyelitis the ready access of effective amounts of penicillin may be prevented because of the relatively avascular nature of the lesion or of the dense fibrous tissue lining the sinus tracts. In these cases surgical intervention is necessary, both to remove as much infected tissue as possible and to allow access of penicillin to the infected area. Adequate surgical treatment in combination with penicillin therapy has been repeatedly stressed in the literature.

A large proportion of cultures of coagulase-positive Staphylococcus aureus are susceptible to penicillin. Some strains of definitely high natural resistance may be encountered. Staphylococci may be made resistant to penicillin by growth in progressively increasing concentrations in broth. Their metabolic activity is retarded, and their pathogenicity is reduced or lost. The coagulase reaction is unaffected. This in vitro resistance is temporary; restoration to sensitivity, but only partial return to pathogenicity, may be effected by serial transfer in broth. Staphylococci may acquire resistance during penicillin therapy. Their metabolic activity is retarded, but their pathogenicity is often unaltered. The coagulase reaction is unaffected. This resistance appears to be permanent.

Penicillin has no effect on the coagulase reaction. It occurs even in the presence of concentrations of penicillin which are ultimately bactericidal. Penicillin has no effect on the formation of staphylococcic alpha toxin and neither enhances nor destroys preformed toxin.

The implication of resistance acquired by staphylococci during penicillin therapy is discussed.

Topical Use of Concentrated Penicillin in Surface-Active Solution.—The available evidence suggests that topically applied penicillin containing 500 Oxford units per cubic centimeter may not be sufficiently concentrated for optimum therapeutic effect in refractory chronic infections.[371] Present pharmacologic purity and possible risk of establishing resistant strains of bacteria by selection justify an upward revision of concentration. Grace and Bryson found definite advantages in the use

371. Grace, E. J., and Bryson, V.: Topical Use of Concentrated Penicillin in Surface-Active Solution, Arch. Surg. **50**:219-222 (April) 1945.

of 4,000 units per cubic centimeter in isotonic solution of sodium chloride with 0.1 per cent of the detergent sodium tetradecyl sulfate for local application to chronically infected areas of bone and soft tissue and for the treatment of infected areas of amputation. If experience in a larger number of cases confirms the efficacy of this simple procedure, it is possible that the magnitude of mutilating major surgical procedures for osteomyelitis may be substantially limited.

Nonoperative Treatment of Osteomyelitis with Penicillin.—Of 7 cases of chronic osteomyelitis involving the extremities, in 3 the hip was affected with either complete ankylosis or limitation of movement.[372] Individual treatment consisted of hospitalization for a period of from ten days to three weeks, with the use of a dosage of intramuscular penicillin (both the sodium and the calcium salt were used) varying from 10,000 to 20,000 units every three hours. In some cases from 20,000 to 50,000 units was used for the first four doses. Simultaneously from 4,000 to 20,000 units of penicillin per cubic centimeter was applied locally into the sinus tract with 1 : 1,000 "aerosol O. T." (dioctyl ester of sodium sulfosuccinate) or "tergitol 4" (sodium tetradecyl sulfate) in isotonic solution of sodium chloride. The local application of penicillin to the site of infection was made at regular three hour intervals with quantities of solution up to 4 cc. retained in each sinus cavity either by drainage or with a compression bandage. The drainage method was accomplished by placing the patient in such a position that the sinus, from its cutaneous opening, would be uppermost, thereby allowing the solution of penicillin and wetting agent to seep down by gravity to the area of infected bone. When this was not possible, petrolatum gauze dressings were placed over the sinus after the solution had been injected.

The authors had one definite failure and in a subsequent publication will present data emphasizing the importance of tracing the location of the sinus opening to the bone with contrast mediums and securing, with minimal surgical intervention, an opening in the sinus directly over this, enabling the optimum amount of solution to reach the infected bone. The simplicity of this principle is demonstrated in case 4, in which the draining sinus was 30 cm. from the infected bone. Prompt results were obtained as soon as the upper portion of this sinus, nearest the primary infection, received adequate penicillin.

Considered cosmetically, the nonoperative method of treating chronic osteomyelitis appears preferable to the older technic of saucerization or sequestrectomy, with its attendant mutilation and prolonged hos-

372. Grace, E. J., and Bryson, V.: Nonoperative Treatment of Osteomyelitis with Pencillin, J. A. M. A. **30**:841-844 (March 30) 1946.

pitalization. In this series alone there had been a total of ninety-one previous operations without any clinical cure.

The removal of all sources of focal infection preparatory to treating patients with penicillin detergent is believed to be of vital importance.

Among war casualties, the high morbidity associated with osteomyelitis of the extremities may be substantially reduced if the effectiveness of nonoperative treatment is borne out by wider clinical experience.

The Management of Osteomyelitis Secondary to War Wounds.—Analysis of Results: An analysis of the results of wound treatment following saucerization by skin grafting, secondary closure and primary closure has been made.[373] No case was considered successful unless the wound had been healed for at least three months. The results with the skin grafting type of treatment have been most satisfactory. A recent survey of 264 cases revealed complete healing of 25 per cent of the wounds in thirty days. At the end of sixty days another 50 per of the wounds had healed, leaving 25 per cent unhealed. Of the latter group, only 6 per cent were complete failures. The remaining patients needed partial resaucerization and skin graft. The failures of this method have been judged to be due to poor blood supply to the tissues under the graft, lack of maintenance of firm even pressure by the dressing after skin graft and lastly to infected tissues under the graft and incomplete saucerization. The skin graft method has been popular with the patients in military hospitals because it created a closed wound from a dirty infected one in a short period, eliminating the dressings, odors and inconveniences of some other methods. Since the soft tissue wounds healed quickly with this method, the bones likewise healed rapidly when they received a covering of skin. However, this treatment did not eliminate altogether the need for further surgical treatment in all the cases. Many deep and wide wounds having a thin skin covering needed good skin flaps with fatty subcutaneous tissues when further bone surgery was planned to keep them from breaking down with usage and for cosmetic reasons. The patients were usually given a trial of three months' hard usage on the extremities if the bones had healed. At the end of that period the patient did not need to undergo further surgical treatment if the skin wounds had not broken down, unless he wanted it for cosmetic reasons.

The results of delayed closure were encouraging, the wounds showing some drainage in 9 of 42 cases which were followed. A number of these wounds closed spontaneously after a few weeks' drainage. The secondary closures, in which a drain was inserted at the time of operation because of a dead space, usually closed spontaneously in the majority

373. Fischer, K. A.: The Management of Osteomyelitis Secondary to War Wounds, Surg., Gynec. & Obst. **83**:507-512 (Oct.) 1946.

of instances within seven to ten days after removal of the drain. The failures in this group of cases were attributed to incomplete surgical treatment and the leaving of a dead space where tissue fluids collected.

Primary closure was used in 46 patients, and wound drainage after surgery occurred in 10 instances. This low incidence of reinfection could probably be accounted for by the proper selection of cases for the use of an immediate closure.

Disseminated Coccidioidomycosis Localized in Bone.—Two cases of disseminated coccidioidomycosis with localized lesions in bone are presented.[374] Both patients are Negroes and give a history of having been stationed in southern Arizona for eleven months.

Complement fixation studies of the patients' serum revealed Coccidioides immitis. Microscopic examination of biopsy material disclosed immature spherules in case 1 and typical, mature spherules in case 2. Cultures of material in both cases yielded colonies of Coccidioides immitis. Mice inoculated with these cultures died, and at autopsy gross lesions were found characteristic of a coccidioidal infection. Mice inoculated with concentrated curettings of the biopsy material died, and spherules characteristic of Coccidioides immitis were demonstrated in the gross lesions, and the organism was recovered from the animals on culture.

The patient in case 2 has since died as a result of disseminated lesions all over the body.

The Several Varieties of Actinomycosis.—In addition to the cervicofacial, abdominal and thoracic forms of actinomycosis, there are other important forms, such as mycetoma.[375] Grains may be absent from lesions, and the actinomycetes may be aerobic as well as anaerobic. The actinomycetes are really higher bacteria.

The diagnosis of actinomycosis can be made by examination of pus or other material and by demonstrating either granules composed of branching filaments or branching filaments in the absence of granules. The anaerobic actinomycete will not be demonstrated by culture frequently since it is hard to grow and usually grown only from granules which have been isolated from pus. The aerobic actinomycete, however, may be cultured more readily, but it should preferably be seen on direct examination of pus or other material, in addition to being seen on culture, in order to know that the organism cultured came from the lesion and was not a contaminant.

374. Sashin, D.; Brown, G. N.; Laffer, N. C., and McDowell, H. C.: Disseminated Coccidioidomycosis Localized in Bone, Am. J. M. Sc. **212**:565-573 (Nov.) 1946.

375. Baker, R. D.: The Several Varieties of Actinomycosis, J. M. A. Alabama **16**:12-14 (July) 1946.

The granules of actinomycosis must be distinguished from the granules of maduromycosis, which have spores, and from the granules sometimes found in staphylococcic pus, which are composed of gram-positive cocci.

The treatment of the deep forms of actinomycosis, especially the abdominal form, has in the past been discouraging to say the least. But it has recently been shown that both the sulfonamide drugs and penicillin are of value. These, in combination with the use of iodides, thymol, surgery, rest and proper nutrition and roentgenologic study in some cases, offer more to patients with actinomycosis than has been available previously.

The Treatment of Chronic Osteomyelitis.—One hundred and forty cases of chronic infections of bone following trauma were studied.[376] Sodium penicillin in the dosage of 40,000 to 50,000 units intramuscularly every three hours was of definite therapeutic benefit. The infections subsided, and the wounds healed, permitting surgical correction of the deformities within six weeks. This saved from five to twenty-four months, the usual recommended interval between the healing of osteomyelitis and any surgical reconstruction for the patient's defects.

Sodium penicillin in lesser doses failed to prevent recurrent attacks of osteomyelitis in these cases when the patients were subject to operative procedures within six weeks after the wounds had healed and the bone infection had subsided. Sulfadiazine also permitted a large percentage of recurrences of the infection after operation.

The penicillin in doses of 15,000 to 25,000 units not only failed to prevent recurrent attacks of osteomyelitis but seemed to be harmful in that the micro-organisms developed a tolerance for this drug. When doses of 40,000 to 50,000 units were later given to the patients, no effect whatever was noted on the virulence of the infection.

Besides the pathogenicity of the micro-organisms in the wounds, many other factors influenced the healing rate. Not the least of these was the state of nutrition of the patients. Most of the patients in this study were suffering from a variable degree of emaciation, secondary anemia and anorexia.

Whole eggs in milk were fed routinely to all patients twice daily between high caloric meals because of the required concentration of amino acids necessary for the reconstruction of the wounded tissues; growth factors must also be supplied to the parasitic bacteria by the patient through the infected bone and other tissues. This may include not only the amino acids, but purines, pyrimidines, oleic acid, vitamins and hemin.

376. Puckett, H. L.: The Treatment of Chronic Osteomyelitis, J. Internat. Coll. Surgeons **9**:581-586 (Sept.-Oct.) 1946.

Penicillin in adequate doses (40,000 to 50,000 units every three hours) is the most valuable therapeutic agent yet introduced in the treatment of chronic osteomyelitis of traumatic origin. Wounds in 94 patients of 100 treated by this method ceased draining and healed after an average of sixty-six days. Twenty patients of this series were operated on for the correction of their deformities within six weeks after drainage had ceased from the osteomyelitis. Some of the surgical procedures were major operations and had to be repeated in stages before the deformities were corrected.

No recurrence of the bone infections was observed after an average of seventy-five days. Previous writers have recommended from six months to two years between the cessation of all signs of bone infection and surgical correction of deformities. By making such corrections within six weeks, not only is much time saved, but the morale of the patient is improved as well as that of other patients awaiting surgical reconstruction.

In Caldwell's [377] first series of 41 cases, there were 16 cases of localized osteomyelitis following compound fracture. Ten tibias, three humeri, two small bones of the foot and one femur were involved. Since then perhaps half as many more have been cared for. The second group of hematogenous osteomyelitis material is more abundant. It contained 12 cases. Five femurs, four tibias, one humerus, one radius and one phalanx were involved.

In the first group of 16 cases, seven wounds were closed with the use of penicillin and six healed per primum. That does not mean that at the first dressing there was absolutely no pus about the stitches, but that within two weeks they were healed and dry. Two wounds were closed without the use of penicillin, both of which broke down. Secondary closures were accomplished in 5 cases; incomplete closure occurred in 1 patient, and 1 deserted.

In the second group of 12 cases nine wounds were closed with the use of penicillin, and they all healed; secondary closures were done on three, and they healed and did not reactivate over a period of a month.

The treatment of chronic osteomyelitis, particularly of the localized type, has been stepped up by surgical procedures that are designed primarily to excise as much of the scar and scarred bone as possible and then to accomplish closure with or without the assistance of skin grafting. Now all of that has been materially improved by the use of penicillin but as much or more so by the proper surgical approach. Caldwell states:

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377. Caldwell, G. A.: Treatment of Chronic Osteomyelitis, J. Omaha Mid-West Clin. Soc. **7**:92-95 (Aug.) 1946.

Likewise, we have been able to close many of the hematogenous type and get primary healing instead of doing, as we formerly did with chronic osteomyelitis, a sequestrectomy, a saucerization and packing with vaseline gauze, permitting it to heal over a long drawn out course and leaving a large scar that frequently broke down. With immediate closure we do not have the large scar, the remaining bone becomes much more healthy and we hope and pray is less likely to break down with abscesses, which give so much recurring trouble.

Cancellous Bone Grafts for Infected Bone Defects.—A Single Stage Procedure: In 52 infected bone defects cancellous chip grafts have been inserted after sequestrectomy and the wound closed, with success in 92 per cent.[378]

The method is applicable in traumatic osteomyelitis and in some cases in which the infection has been blood borne. No virulent infections have resulted, and there has been no flare-up of infection after healing for periods up to fourteen months.

In a small series in which traumatic osteomyelitis involved joints, chip grafts have been used after sequestrectomy, with healing and satisfactory fusion. Successful chip grafting in the presence of infection depends on (*a*) complete sequestrectomy and removal of all infected tissue; (*b*) an adequate vascular bed for the grafts which must have all cortex removed; (*c*) no dead spaces; (*d*) penicillin, systemically and locally, with sulfonamide therapy if indicated; (*e*) full thickness skin to close any skin defect, and (*f*) plaster immobilization (for soft tissue healing and until the bone is consolidated).

The one stage method for obliterating infected bone defects saves months of hospital treatment and restores function before disuse changes become irremediable.

The Use of Penicillin Therapy in Conjunction With Free Bone Grafting in Infected Areas.—Eight patients have been studied in whom free bone grafts have been implanted successfully in infected defects in bones in conjunction with penicillin treatment.[379] Seven of these patients had infected fractures of large bones of the lower extremity with nonunion, and 1 had a contaminated defect resulting from an extensive resection of bone following removal of a secondarily infected tuberculous knee joint. The pathogenic bacteria cultured from the wounds of these patients were hemolytic Staphylococcus aureus in 4 cases, beta hemolytic streptococcus and hemolytic Staph. aureus in 2 cases, Escherichia coli and hemolytic Staph. aureus in 1 case

378. Coleman, H. M.; Bateman, J. E.; Dale, G. M., and Starr, D. E.: Cancellous Bone Grafts for Infected Bone Defects, Surg., Gynec. & Obst. **83**: 392-398 (Sept.) 1946.

379. Abbott, L. C.; Bost, F. C.; Schottstaedt, E. R.; Stern, W. E., and McCorkle, H. J.: The Use of Penicillin Therapy in Conjunction with Free Bone Grafting in Infected Areas, Surg., Gynec. & Obst. **83**:101-106 (July) 1946.

and Streptococcus viridans and hemolytic Staphylococcus albus in 1 case. Penicillin was given intramuscularly at three hour intervals before operations in 5 of the cases and after operations in all the cases. The dosage varied from 100,000 to 200,000 units per day. Prolonged treatment extending over many weeks was necessary. The total amount of penicillin used in each of these cases varied from 3,000,000 to 8,000,000 units.

The free bone grafting operations consisted of insertion of iliac grafts and metal plates (4 cases), sliding bone graft and metal plates (1 case), iliac grafts without metal fixation (2 cases) and sliding bone graft without metal plating (1 case). The operative wounds were closed completely in 7 cases, and in 1 case the wound was closed around a small soft rubber tube through which supplementary treatment with local penicilin was given. The most recent bone grafting operation had been done three months previously, and this wound had not yet been inspected, but there were no signs of infection and the patient left the hospital with plaster fixation. Immediate primary healing resulted in 4 cases; however, in 1 of these cases an adjacent sinus tract reopened after the operation and drained temporarily, and another patient returned for treatment of an infection that developed six months after operation. In 2 wounds necrosis and low grade infection resulting from tension developed at the site of closure, and these have required secondary closure and skin grafting procedures. One wound became infected and required drainage, but the patient was receiving inadequate doses of penicillin at the time.

At present the wounds of 6 of the 7 patients with grafting operations for infected nonunited fractures are healed completely, and 1 (which became infected six months after operation) is under treatment. On roentgen examination, the bone grafts in all these cases appear to be viable and in proper position, but 1 graft in a defect of the tibia fractured four months after operation and required a supplementary (fibular transplant) procedure. None of the grafts has sequestrated, extruded or has been absorbed. Four patients have firm union of the fracture sites, with metal plates still in position, and 2 have firm union without metal plates. One patient has not yet had the original plaster dressing removed, and the remaining patient is the one for whom fibular transplant was required because the graft in the tibial defect fractured four months after the bone grafting operation.

Even though it has been possible under penicillin therapy to accomplish free bone grafting directly into the infected bone defects successfully in these cases, it is probably more desirable in most instances to attempt to obtain healing preliminary to the grafting procedure by penicillin therapy and, if necessary, by operations for removal of sinus tracts, infected granulations, scar and nonviable bone. The bone

grafting may then be accomplished at a later operation in a relatively cleaner field. Adequate dosage with penicillin is a useful adjunct in all cases in which bone grafting and other operations are done in areas in which there are bone defects infected with penicillin-susceptible organisms.

Skin Grafting in the Treatment of Osteomyelitic War Wounds.—During the past three years Kelly [380] witnessed at close range the application of skin grafting technics to the healing and subsequent treatment of osteomyelitic wounds. There is little basic difference between closure by skin grafts, either free or pedicled, and secondary or primary closure as advocated by Key, Dickson and his associates, Churchill and Hampton during the war and the years which immediately preceded it. In some war wounds loss of both bone and soft tissue is so extensive that it precludes secondary closure, and some other means must be sought for inducing prompt healing. Free skin grafts will often effect healing of such wounds.

At Ashford General Hospital this work has been carried out in an orthopedic section manned by officers whose training has been in orthopedic surgery or general surgery or a combination of the two. A concerted effort has been made to satisfy the principles of skin transference, with especial reference to the avoidance of tension and the development and protection of the blood supply in pedicle grafts. In some instances the technic which could be applied to the task was inadequate to meet such basic requirements in the circumstances which arose. Obviously, these instances represent failures. These failures are in some measure offset by the prompt, good results obtained in the predominating group and by appreciation of the severe problems presented by some cases. Because of the tremendous number of battle casualties, the skill of the army plastic surgeon will not be available to many patients with osteomyelitis for several years. The orthopedic surgeon, with an understanding of the basic principles of skin transference but usually with little training in its details, will have to face some of these problems. It is the author's intent to present an abstract of the experience of the group with which he has been associated in this work.

The technic of plastic surgery can be applied to treatment of certain types of osteomyelitic wounds. Success in producing healing by free skin grafting has been considerable. Later stages of reconstruction in these instances have succeeded, often in proportion to the operator's facility in performing pedicle skin transplants. In replacing free skin grafts with pedicles in this group of patients, dead space presents a major problem. Contrary to the experience of others, attempts at Ashford

380. Kelly, R. P.: Skin-Grafting in the Treatment of Osteomyelitic War Wounds, J. Bone & Joint Surg. **28**:681-691 (Oct.) 1946.

General Hospital to fill such cavities with iliac bone chips have resulted in a high proportion of infection; other filling materials have been used, with varied success.

Leonard T. Peterson called attention to the fact that the technic described by Colonel Kelly has been limited to observation of the orthopedic surgical procedures at a number of army hospitals. In the early months of the war it was customary to treat chronic osteomyelitis for long periods with plaster and infrequent dressings. Often the surgeon was reluctant to carry out the treatment required for adequate drainage and removal of sequestrums.

A more aggressive attitude has been taken with the excision of sequestrums and other devitalized tissue, followed by early skin grafting. Secondary closure of the wounds, without preliminary skin grafting, has not usually been successful. The development of early saucerization, followed by skin grafting, parallels closely the early secondary closure of compound wounds, as developed especially in the Mediterranean Theater and later practiced in all theaters.

The method represents one of the most important developments in reconstructive surgery of the war.

Repair of Bony Defects Associated with Osteomyelitis.—Chronic, localized hematogenous osteomyelitis continues to present a difficult surgical problem.[381] Infection is harder to control in bone than in other connective tissues. Bone is rigid, its vessels cannot contract or expand and its cavities do not collapse. Even if infection has finally been arrested, the surrounding bone is abnormal because of diminished circulation, increased density, loss of valuble organic material and isolated tiny cavities containing dormant organisms.

The advent of chemotherapy and the development of new procedures in the management of compound fractures during the war gave rise to the hope that osteomyelitis might be eliminated. As the end results of treatment become better known, it is evident that chemotherapy is not the entire answer to the problem and that well directed surgical measures must continue to be the mainstay for the treatment of chronic osteomyelitis.

A project, under the direction of the Subcommittee on Wounds and Burns of the National Research Council, was undertaken to evaluate various surgical procedures for the repair of bony defects associated with chronic osteomyelitis. The objects were to promote union of compound fractures with bony defects and infection and to obtain closure and healing of the infected bony cavities in chronic hematogenous osteomyelitis.

381. Caldwell, G. A.: Repair of Bony Defects Associated with Osteomyelitis, Ann. Surg. **123**:698-701 (April) 1946.

Well directed surgical measures to remove dead bone, flatten cavities and obtain good soft part coverage of the remaining bone continue to be the mainstay for the treatment of chronic osteomyelitis. Penicillin and sulfonamide drugs play only a limited role in the elimination of infection and in final healing. Of 21 patients with localized osteomyelitis treated by various surgical procedures supplemented by chemotherapy, in 80.9 per cent the wounds healed per primum, but in only 61.8 per cent did they remain healed after five to twelve months. Of 22 cases of hematogenous osteomyelitis, again the wounds healed primarily in 81 per cent and, in 63 per cent they remained healed after five to twelve months.

Dr. William Darrach, in a discussion on Caldwell's [381] paper, said:

I should like to emphasize one point brought out that we as civilians have to face, and the men in the army and naval hospitals have to face; that is, the filling in of defects following gunshot or other wounds of the lower extremities, more especially the tibia. There is an underlying principle they have mentioned, which Champ Lyons brought out several years ago, and others have since—that is, the preparation of the patient prior to operative work in the final stage of treatment to fill in these defects. I think one of the most graphic descriptions of preparation of the patient comes from the Bible. . . .

If we are going to prepare any form of bone graft or filling-in of a cavity, we must pay attention to preparation of the patient from both a general and local standpoint. It is interesting to see how reparative bone processes will improve after a few transfusions; building up the patient from all points of view, general as well as local preparation, will determine very largely the success of our efforts.

Dr. Norman T. Kirk: Wounded casualties in the Army amounted to approximately 571,000, of whom about 360,000 were returned to duty overseas. About 25,000 of our wounded died, approximately 4 per cent. I am told on good authority that the German losses in this category amounted to 8 per cent, and that during the winter campaign of 1944-45 about 13 per cent of their wounded died as a result of their injuries.

In my own mind there is no doubt why the percentage of American deaths from wounds was so much lower than the German percentage. I was in North Africa in April, 1943. I was in Italy the following year. What happened in the Medical Corps between those two dates is the explanation.

On the occasion of my first visit to the Mediterranean Theater of Operations, every medical officer in the Corps was treating patients, according to his own plans and policies. Some of the methods were very good. Others, to put it bluntly, were very poor. On the occasion of my second visit, every patient in the Theater was being treated according to the definite regimen instituted under the leadership of Colonel Churchill. Phases of military surgery and the missions of each echelon in respect to them had been clearly established. The first phase, initial surgery, was performed near the front lines. The second phase, reparative surgery, was performed in the Base Hospital behind the lines. The third phase, reconstructive surgery, was performed in the Zone of Interior.

It was this system of surgery, strictly adhered to, which gave the American Army the lowest percentage of deaths from wounds ever achieved in any Army. Before this method was developed, to give you a single illustration, the incidence of osteomyelitis following compound fractures was relatively quite high. Initial débridement was often imperfectly done, and delayed wound closure was infre-

quently practiced. Patients were put in plaster and arrived in this country with infected, malodorous wounds, the end-result of which was deformity.

Then the plan was changed. Initial surgery was thoroughly carried out in Field and Evacuation Hospitals. Primary closure was not permitted. It was impractical to secure precise reduction of fractures in the Forward areas, and the attempt was therefore not made. Instead, plaster designed primarily for transportation from the Forward Hospital was applied and the patient was transferred to the General Hospital in the Base. Once he reached the General Hospital, accurate reduction was achieved by manipulation or skeletal traction. The compounding wounds, if they were clinically clean, were closed by suture or skin graft, usually within five to ten days after wounding.

Patients were held in the Base Hospital until early callus formation would prevent displacement of their fractures during transportation. Those with fractures of the femur were held for eight to ten weeks, and sometimes longer, in skeletal traction. Then, in a lag-period, when no definitive surgical procedure was necessary, they were transported to the Zone of Interior.

Let me call your attention to several special points. In the first place, please note that it was the gross appearance of the wound which determined the time for delayed suture or skin graft, not bacteriologic studies. I yield to no one in my admiration for the bacteriologist in his place, but I thank God he was not available for use in this connection.

In the second place, while great advances have been made in reconstructive bone surgery, I do not myself classify a sliding bone graft of the tibia among them. I sometimes hear surgeons remarking that they can perform such grafts and "get away with them." Perhaps so, though not in most cases, and I do not believe, regardless of the outcome, that this method represents good surgery. Furthermore, we learned in the course of the war, and it is regrettable that we had to learn it over again at the patient's expense—we knew it 25 years ago—that any kind of graft is useless unless it is put into a properly prepared bed.

Finally, let me say a word about chemotherapy. We owe much to the sudies of the National Research Council in this field, and the systemic administration, first of the sulfonamides and later of penicillin, undoubtedly saved many lives. . . .

All our badly wounded soldiers—between 260,000 and 280,000 of them—have been brought back to the General Hospitals in this country. The men with osteomyelitis, the men with bilateral amputations, the men who need multiple plastic operations and multiple hand surgery and other equally serious procedures have come home from the war. Their need now is primarily for specialized treatment. The fighting war is over, but the Medical Corps has still a job to do. That it will be finished with the same competence with which it was begun, I have not the slightest doubt.

DR. DUANE CARR: Over a number of years it has been my privilege to observe a reasonable number of patients with osteomyelitis of the bones of the thoracic cage. It is a problem on which Dr. John Alexander and I wrote some 10 or 12 years ago and at that time we advocated adequate surgical débridement of the tract followed by primary closure in those cases of tuberculous osteomyelitis uncomplicated with pyogenic infection. However, many of these cases of osteomyelitis of the sternum, ribs or clavicle were primarily tuberculous but complicated with pyogenic infection, following incision and drainage of the original abscess, resulting in a chronic mixed infection.

In our 46 cases a fairly large percentage of those treated with primary closure reopened. Many of our earlier mistakes, I believe, have now been overcome. Our practice now is the complete excision of all infected tissue and bone followed by primary closure with a pressure dressing, even in the mixed infected cases. Peni-

cillin before and after operation is a helpful adjunct, but we found our principal mistake formerly was in failing to carry out a more complete excision. Osteomyelitis of the thoracic cage complicated by tuberculosis has a tendency to develop sinuses boring through adjacent tissue and leading to other abscesses at some distance from the site of the original infection. Many of these sinuses are so small as to escape detection in the operative wound. I have, therefore, routinely used the injection of one per cent methylene blue under gentle pressure before the excision is begun and, to be complete, the excision must include all stained tissue. A spot less than one millimeter in diameter may be a sinus leading to an abscess elsewhere or even osteomyelitis of adjacent bony structures.

The use of methylene blue, the complete excision of all diseased tissues, primary closure without drainage, a pressure dressing, and penicillin before and after operation, have resulted in 100 per cent permanent closure in the limited number of patients so treated in the past two years.

DR. CHARLES S. VENABLE: I have enjoyed the very scholarly presentation of Doctor Caldwell and am for once not in any disagreement. I think, however, there are some few very salient factors that may be taken in their order in doing secondary rearrangement and rehabilitation following destructive osteomyelitis. General Kirk "rang the bell" when he said you cannot expect sulfa and penicillin to take all the cockroaches out of the kitchen. It takes plenty of good surgery, as we learned in the last war. Let us grant this has been done and we come to the defects following osteomyelitis. I think we must give the time-element a sufficient waiting period to know that no further necrosis is beginning in the bone ends. That gives an expression of the blood supply, because if this is insufficient, union will not take place. When this has been decided—the condition of the tissues and even spots of regeneration of bone—the remaining periosteum must be removed and the bone ends denuded entirely to assure the blood supply to both ends of the graft. This must be firmly fixed, because if there is movement, fibrosis will occur at one or the other end and union will not take place. I think soft-tissue closure is almost as important because, after all, blood supply is what it takes; closure of the soft-tissue so closely and completely about the graft that it may pick up blood supply between its ends. A dead space there is an exposure to defeat.

DR. ROBERT W. JOHNSON: My introduction to chronic osteomyelitis took place at the hands of Doctor Halsted. In those days we were sterilizing these cavities after radical excision and saucerization by pure carbolic acid, followed by alcohol, and lavage with at least ten gallons of bichloride solution. With his meticulous technic the field was cleaned and redraped, and we transferred to an entirely clean instrument table and set-up. Even after this heroic procedure the blood clot would break down and the wounds show the same organism as before. The experience sold me on the idea that the wound of an osteomyelitis could not be sterilized by any local method, and later experience with Dakin's solution, maggots, sulfa compounds, and penicillin locally have only served to confirm this. We have, however, an entirely new help in systemic chemotherapy, working on the "patient-side" rather than the "doctor-side" of the wound. This is the greatest advance that has been made, and this change in method and point of attack has been shown splendidly by the essayists.

I think that Doctor Caldwell's slides on the pathology, with which he introduced his remarks, are the crux of the situation. He shows that he is dealing with the pathologic tissue and not the cavity. The cavity is one thing, the pathologic tissue in the wall of the cavity is another, and this latter is what we must keep in primary consideration. We are dealing with tissue, ill-supplied with blood at best, which has little chance to become hyperemic, and with bone trabeculae and scar-filled

spaces it has little power of healing. This is why bone cavities differ from other scars in healing ability. New blood supply is simply unable to reach the site of the disease. While this is true in acute osteomyelitis, it is ten times more so in the chronic type. All the measures that have been suggested are of value—grafts of skin, flaps, muscle flaps, *etc.*, in that they reduce the area to be filled in and/or bring with them new vascular supply to aid in the process. Major Kelly's cases which we were privileged to see yesterday, are even more convincing than his excellent paper of today.

DR. FREDERIC W. BANCROFT: I would like to emphasize the difference in the healing of fractures of bone and ordinary connective tissue. Bone consists of two elements: a cellular element and a matrix which has low metabolic needs and can persist for a considerable time without the presence of cellular elements. When a bone transplant is imbedded, sections of this bone two or three weeks after operation will show the absence of osteoblasts in the bone spaces. As time goes on, if graft is to succeed, there will be revascularization through the vessels entering the Haversian canals and about these vessels will appear numerous bone cells in the canaliculi. If revascularization does not occur in the bone graft and cells do not reappear, the bone eventually atrophies, or if infection be present it is cast off as a sequestrum. I believe that we see the evidence of bone atrophy in late fractures of the graft when the transplant is not laid in a vascular bed.

These observations are important clinically because they show us that we must place a graft in an area free from scar tissue and infection if we expect the graft to persist and become living bone, which occurs by a gradual process of creeping replacement.

Chemotherapy in Surgery.—A brief review of the usefulness of chemotherapeutic agents (sulfonamide drugs, penicillin, streptomycin) in surgery is presented.[382]

Their principal uses are prophylactically to reduce the hazard of surgery in contaminated operative fields, primary therapeutic use with limited procedures and secondary therapeutic use as an adjunct to surgical treatment.

Systemically administered sulfonamide drugs and penicillin may be given to prevent invasive wound sepsis from streptococcic and staphylococcic infections in accidental wounds and burns and in operative wounds.

Orally administered succinylsulfathiazole, phthalylsulfathiazole and streptomycin may be useful adjuncts to surgery of the gastrointestinal tract.

Combined penicillin and streptomycin, administered systemically, by inhalation or by instillation, is suggested as a means of reducing infection in surgery of the lung. Streptomycin alone may prove a valuable adjunct to the surgical treatment of pulmonary tuberculosis.

For the treatment of invasive infections, penicillin in doses of 400,000 to 1,200,000 units daily is recommended. Patients with peritonitis should also be given streptomycin (1.5 to 2 Gm. daily). In

382. Lockwood, J. S.: Chemotherapy in Surgery, J. A. M. A. **135**:747-749 (Nov. 22) 1947.

infections involving a joint or the pleural cavity, pus should be aspirated and replaced with penicillin solution (5,000 to 20,000 U./cc.).

Infections which may respond to chemotherapy alone are listed as follows: cellulitis, lymphangitis, bacteremia; acute hematogenous osteomyelitis; suppurative arthritis; acute thoracopulmonary suppuration; spreading peritonitis; furuncles and carbuncles.

Infections which certainly require both chemotherapy and surgery are as follows: acute appendicitis with local peritonitis; chronic osteomyelitis; infections of the hand and foot, with or without diabetes; bronchiectasis, chronic empyema and pulmonary abscess; gas gangrene; chronic granulomas, including actinomycosis.

The usefulness of sulfonamide drugs, streptomycin and particularly penicillin in the treatment of surgical infections is discussed.[382a]

Sulfonamide drugs have proved useful in acute infections caused by the hemolytic streptococcus, pneumococcus and gonococcus but have been of little or no value in those due to the hemolytic staphylococcus. The limitations of sulfonamide therapy include inactivity in pus, wound exudates and necrotic tissue, bacterial resistance and the development of drugfastness by bacteria, toxic reactions and drug idiosyncrasy.

Penicillin therapy is largely without these limitations.

Neither sulfonamide nor penicillin therapy will prevent the development of local infection in contaminated wounds, but both may inhibit or control any infection which develops, thus preventing invasive infection. Since penicillin is effective against staphylococci, which usually cause wound infections, it is superior to the sulfonamides.

Between November 1942 and February 1947, 754 surgical infections were treated with penicillin; 465 were established staphylococcic infections. It is concluded that "penicillin is the chemotherapeutic agent of choice in the treatment of all staphylococcal infections in surgery and that it has replaced all previous forms of chemotherapy."

In early diffuse infections, penicillin therapy frequently produced complete and spontaneous resolution. When treatment was begun later, frequently the infection was localized, obviating the necessity for radical operations.

The mortality in 40 cases of staphylococcic septicemia treated between 1940 and 1942 with sulfonamide drugs, surgery or bacteriophage was 67.7 per cent, while that in 51 cases between 1943 and 1946 in which penicillin was given was 30 per cent. Penicillin therapy "was most successful in young adults or children in whom the diagnosis of staphylococcal bacteremia was made early, penicillin therapy given early and intensively, and surgical drainage was possible when indicated."

382a. Altemeier, W. A.: Chemotherapy in Surgery, J. Missouri M. A. **44:** 803-809 (Nov.) 1947.

Penicillin is also "the chemotherapeutic agent of choice" in the treatment of carbuncles. Among 54 patients treated between 1944 and 1946 with 15,000 to 20,000 units intramuscularly every three hours for an average of seven days, there was complete spontaneous resolution in 27.7 per cent, partial resolution with necrosis in 22.2 per cent, abscess formation in 44.4 per cent and failure in 1.8 per cent.

"Penicillin is a powerful and effective chemotherapeutic agent in the management of acute osteomyelitis, and it has greatly modified both its management and roentgenographic interpretation." When adequate treatment was started within the first two or three days, surgical intervention was usually unnecessary and abscess formation was rare. When treatment was delayed for seven to ten days, there was extensive bone destruction, abscess formation and sequestration.

Among 59 cases of chronic osteomyelitis, spontaneous resolution occurred in only 9. Surgical treatment was required in the remainder.

Penicillin proved far superior to the sulfonamide compounds in the treatment of anaerobic streptococcic infections and was effective in sulfonamide-resistant hemolytic streptococcic infections.

In pneumococcic infections, penicillin was reserved for those that were sulfonamide resistant. Excellent or good results were obtained in 48 of 70 cases.

No beneficial effects were observed with penicillin in 22 cases of established generalized tetanus.

Penicillin proved "a valuable therapeutic agent" in 9 cases of human bite infections.

Excellent results were obtained with penicillin therapy in 3 of 4 cases of the streptobacillary type of rat bite fever.

"Penicillin is by far the chemotherapeutic agent of choice in the treatment of gas gangrene." Large doses of penicillin (1,000,000 units every three hours) together with adequate surgery are necessary for successful results.

Best results in actinomycosis are achieved by penicillin in full dosage for four to eight weeks together with sulfadiazine continued for four to six months.

Infections due to organisms susceptible to streptomycin therapy occur less frequently than those due to organisms susceptible to penicillin. Successful streptomycin therapy depends on the use of large doses from the beginning to prevent the development of organism resistance and early surgical drainage of abscesses before such resistance occurs.

Development of Bacterial Resistance to Antibiotics.—The development of resistance to the antibiotics is a phenomenon of great theoretic interest to the bacteriologist, and it may some day become a matter of

major concern to the clinician.[383] Miller limits his discussion to penicillin and streptomycin, the two antibiotics which have been most intensively studied clinically and experimentally and about which, therefore, a good deal of information has accumulated.

Penicillin resistance when it does develop proceeds slowly. It has not as yet become a serious clinical problem because most infections are brought under control before any appreciable degree of resistance has had time to develop and also because most patients at the present time receive doses of penicillin sufficiently in excess of the minimum required to take care of any increase in resistance which might occur during the course of their treatment.

Streptomycin resistance, on the other hand, can develop with great rapidity. This has been observed clinically as well as experimentally. It is probably due to the production by bacteria of streptomycin-resistant variants which arise by mutation. Such variants have been described for several bacterial species. In the case of Meningococcus, two streptomycin-resistant variants have been observed, one of which is remarkable in that it requires streptomycin for its growth in vitro and in vivo.

Penicillin in the Treatment of Chronic Osteomyelitis.—The response to penicillin therapy in chronic bone infections was not dramatic.[384] The initial injury followed by a low grade infection produces fibrosis and results in impaired local circulation. As the condition becomes more chronic, osteomyelitic cavities become sclerosed, preventing the penicillin from reaching the diseased area in adequate concentrations, and since sequestrums have no blood supply it is practically impossible to sterilize them.

In this study of 58 patients with chronic bone infections, some of which were treated with penicillin alone and some with penicillin and surgery, certain facts were found which the authors believe are worthy of note.

(1) Penicillin by inhibiting the growth and multiplication of bacteria will arrest infection in cases of chronic osteomyelitis with no sequestrums and in a high percentage of cases will allow healing to take place within a short time after the administration of the drug. In 64 per cent of the authors' cases the infected areas closed under specific therapy and with specific therapy and surgical treatment.

(2) Penicillin is of definite value in decreasing postoperative complications. There was none in their group of patients operated on.

(3) With adequate systemic penicillin therapy, the local administration of the drug is unnecessary and even undesirable.

383. Miller, C. P.: Development of Bacterial Resistance to Antibiotics, J. A. M. A. **135**:749-751 (Nov. 22) 1947.

384. Kaplan, I. W., and Bauer, G. H.: Penicillin in the Treatment of Chronic Osteomyelitis, Texas State J. Med. **42**:202-204 (July) 1946.

(4) Pyocyaneus was present in 16 of the 21 cases in which the patients did not respond favorably to penicillin therapy and may well be one of the important causes for failure.

(5) The presence of mechanical factors, such as fibrosis, sequestrums and sclerosis of bone, all influence the efficacy of penicillin. Because of the decreased vascularity of the diseased area and of the nontoxicity of the drug, it is recommended that comparatively large doses of penicillin be administered, 240,000 units daily, in an effort to increase the local concentration in the affected area.

(6) The use of penicillin will not obviate the need for surgical treatment. Sequestrums when present must be removed. In a small number of cases the infection might have healed without specific therapy during the five month period covered by this study. The authors are also aware of the fact that some of the wound closures do not represent cures and may later break down.

The treatment of chronic osteomyelitis is a problem not yet successfully solved.[385] In modern surgery the problems have revolved around (*a*) the extent to which diseased bone should be removed; (*b*) the time at which to perform operation; (*c*) the method of filling in bone defects, and (*d*) the method of treatment before and after operations.

An investigation was undertaken at Christie St. Hospital, Toronto, Canada, in October 1943 to study the effects of penicillin in the treatment of chronic osteomyelitis resulting from compound fractures or blood-borne infection. Of the 57 patients in this series, who were initially treated between October 1943 and August 1944, 43 had septic compound fractures following battle wounds or accidents, while 14 had disease of hematogenous origin. Fifty cases have been followed to December 1945.

In the first six weeks of the investigation, penicillin therapy was used alone. As the results of this initial study were disappointing, surgical measures were also used in subsequent cases when indicated.

The effect of penicillin alone is described in cases of chronic osteomyelitis with sequestrums, cavities or other conditions for which surgical procedures are usually carried out. The results were poor.

The effect of penicillin alone is described in cases which did not require operation or in which operation was contraindicated. Of 5 such cases, complete healing occurred in 3 and great improvement in 2.

The effect of penicillin combined with surgical procedures is described. Of 52 patients, 43 are completely healed and 9 are unhealed. There were 24 patients who had recurrences after the first operation.

Results are given in 50 cases followed for fifteen to twenty-five months.

385. Hebb, H. D.: The Role of Penicillin in the Treatment of Chronic Osteomyelitis, Canad. M. A. J. **54**:446-450 (May) 1946.

It is recommended that penicillin be used in the treatment of chronic osteomyelitis. In most cases, its use should be combined with adequate surgical treatment both before and after operations.

It is recognized that final assessment of treatment cannot be made for many years because of the nature of the disease.

The Treatment of Chronic Osteomyelitis by the Use of Muscle Transplant or Iliac Graft.—Prigge [386] presents the method used in treating sixty-four separate foci of chronic osteomyelitis in 61 patients during a period of sixteen months. Practically all areas of the skeleton were affected. In 4 cases major joints were involved with suppurative arthritis. Healing occurred in a high percentage of cases within ten weeks, and there have been no recurrences, pathologic fractures or fatalities. The average period of observation was seven and one-half months. All patients were males between 18 and 37 years of age. The disease was due to the usual causes, being hematogenous in 4, secondary to operative infection in 6 and secondary to infected compound fractures in the remainder. The chronic granulomas of bone are not included in this series, although this method should be applicable in selected cases of this type of chronic bone infection.

The management of chronic pyogenic osteomyelitis is one of the most distressing problems in the field of orthopedic surgery. Whether it is secondary to infected compound fractures or to operative infection or whether it is hematogenous in origin, the bone infection has been difficult to eradicate. Too often it results in crippling from stiffened joints, atrophied muscles, recurrence of the disease, pathologic fractures and occasionally delayed union or nonunion of infected fractures. The chronic sepsis enforces an interminable delay in undertaking reconstructive surgery. Frequently, it is the direct cause of secondary anemia and the rare, but serious, complication of amyloid degeneration. Nephrolithiasis is not an uncommon finding in debilitated patients, particularly when prolonged recumbency is necessarily enforced. If there is a lesion of a peripheral nerve, associated with a compound fracture—as is frequently seen, due to the perforating, high speed missiles of modern warfare—it is imperative to clear up infection early, in order that definitive neurosurgical procedures may be accomplished without delay. The longer the time interval between laceration of nerve tissue and surgical repair, the poorer is the prognosis for recovery of the paralyzed muscle groups.

The advent of the bacteriostatic drugs, particularly penicillin, at first gave promise of a possible cure. However, it soon became apparent

386. Prigge, E. K.: The Treatment of Chronic Osteomyelitis by the Use of Muscle Transplant or Iliac Graft, J. Bone & Joint Surg. **28**:576-593 (July) 1946.

that penicillin, like the sulfonamide drugs, would not be effective, either systemically or locally, in tissues with little or no vascularity. Such tissues include sinus tracts with the surrounding cuff of dense scar tissue, bone abscesses containing chronically infected granulation tissue, sequestrums and areas of eburnated bone which are frequently found at sites of chronic osteomyelitis. Furthermore, the newer bacteriostatic drugs, such as streptomycin, could hardly be expected to accomplish better results after chronic bone infection has become established. The value of these drugs as adjuvants to the surgical treatment of osteomyelitis is considerable, however, since more radical surgical procedures are possible without danger of the localized infection becoming disseminated or assuming an invasive character. In all the cases reported here, penicillin only was used, as it is less toxic than the sulfonamide drugs. Streptomycin was not available.

The prompt and permanent healing of chronic pyogenic osteomyelitis is imperative, in order to prevent the many serious complications and sequelae and to permit early reconstructive surgical intervention when necessary. With the present day bacteriostatic drugs, more radical procedures can be accomplished without danger to life or limb.

Sixty-four separate foci of chronic osteomyelitis in 61 male patients between 18 and 37 years of age have been treated during the past sixteen months. Early healing (within ten weeks) occurred in 78.1 per cent. Including the 8 cases in the iliac graft series, in which healing was delayed over the ten week period, and the case in which reexcision was necessitated by a secondary sequestration, complete healing occurred in 93.7 per cent.

The method used and advocated is founded on the principle of complete excision of an infected and avascular tissue, obliteration of the "dead" space and wound closure. Whenever possible, obliterating the dead space with viable muscle has been the method of choice, since 97.7 per cent of the wounds in this group healed promptly. Bone grafting should be done later, if necessary, to reenforce any bone weakness. In the calcaneus, the anterior surface of the tibia and the radial styloid, obliteration of the dead space with grafts of cancellous iliac bone has shown definite merit and has been time saving.

Bone Felon.—Drawings were presented by Lovejoy [387] to show the severe disabilities from a relatively simple condition in 4 cases and to suggest a means of avoiding this disability.

A plea is made for the early diagnosis of this condition and for lateral drainage. This will prevent a painful, disabling scar on the digital pad. A double lateral incision with through and through drain-

387. Lovejoy, J. F.: Bone Felon, U. S. Nav. M. Bull. **46**:1465-1466 (Sept.) 1946

age is often indicated and easily accomplished. The optimum time for drainage can be readily determined by careful daily observation. Even though there is a tendency for the abscess to point through the digital pad, this can be averted by a lateral incision. Chemotherapy is indicated preoperatively and postoperatively. The local use of penicillin has been found advantageous in the experience of the writer.

Penicillin and Bone Grafting Operations.—Among 3,000 war fractures it was deemed advisable to perform bone graft operations, in order to facilitate union, in only 93, or 3 per cent.[388] Fifty of these operations were performed before penicillin was available for their use. Forty-three operations have been performed utilizing penicillin.

The purpose of Branch and Moldavsky's article is to offer an analysis of these 93 bone graft operations on war fractures so that a comparison will be available of the end results of those operations done without penicillin and those in which penicillin was utilized.

Of 3,000 war fractures treated, it was necessary to use bone graft in only 93, or 3 per cent, to obtain union. Of these 93 bone graft operations, there were 50 done without utilizing penicillin and 43 in which penicillin was utilized.

Statistics, case reports and discussions of these 93 bone grafted fractures have been given so that a comparison may be drawn between operations performed without penicillin and operations in which penicillin was utilized. There has been a special effort to make readily available the statistics on postoperative wound healing in cases in which operation was performed without penicillin and in those in which penicillin was utilized.

Infection in the 8 postoperative cases remained localized, but bone grafts were lost in 2 cases when penicillin was not given and in only 1 case when penicillin was administered.

In this series the infection was less disturbing and the wound healing results were best in cases in which administration of penicillin was started two days before operation.

The Treatment of Extensive Actinomycosis.—Interest in the problem of the treatment of extensive actinomycosis was aroused by a case of advanced abdominal actinomycosis occurring in a young girl.[389] Over a period of several months, the progress of the disease was arrested and the patient rehabilitated to a normal life and probably cured. A review of the hospital records revealed that although the results from the treatment of mild or early actinomycosis by a variety of

388. Branch, H. E., and Moldavsky, L. F.: Penicillin and Bone Grafting Operations: Evaluation of Operations Performed Without Penicillin and Those Performed with Penicillin, Mil. Surgeon **99**:25-31 (July) 1946.

389. Kolouch, F., and Peltier, L. F.: Recent Advances in Surgery: Actinomycosis, Surgery **20**:401-430 (Sept.) 1946.

therapeutic agents were good the treatment of advanced actinomycosis was uniformly unsuccessful. With this in mind, the case records have been carefully examined and compared, and a review of the literature has been made. The collected information has been used as a basis for an evaluation of the treatment of extensive actinomycosis.

The results in the treatment of cervicofacial actinomycosis show a close correlation between the extent of the lesion at the time treatment was instituted and the eventual prognosis. The results in the treatment of thoracic and abdominal actinomycosis have been poor. The success with the last case, however, indicates that the prognosis for any of these patients should not be hopeless.

Success in the treatment of actinomycosis depends to a large extent on early diagnosis of the condition since circumscribed lesions will respond satisfactorily to any of the recognized forms of treatment. Extensive involvement, irrespective of location, presents a serious

Results of Treatment of Cervicofacial Actinomycosis in 16 Cases Classified as to Type

Type	Number	Cured	Healing	Dead
1	7	5	2	0
2	6	5	..	1
3	3	..	..	3

threat to the life of the patient and a challenge to the ingenuity and perseverance of the physician.

Cervicofacial actinomycosis has proved relatively amenable to irradiation, surgery or chemotherapy. The mortality of this type of infection results from extensions of the infection into vital structures. Repeated excision and curettage as emphasized by Wangensteen appears to be the treatment of choice in extending infections. Adjuvant chemotherapy enhances the possibility of success in the extensive lesions treated by surgical measures.

Thoracic actinomycosis has been notoriously resistant to treatment prior to the advent of modern chemotherapeutic agents. The sulfonamide drugs and penicillin should bear the burden of treatment in these cases. Surgical procedures should be limited to the drainage of collections of pus and the excision of grossly infected tissue.

Results in the treatment of abdominal actinomycosis have been generally poor. Irradiation therapy of these lesions has been limited by the technical difficulties encountered in applying the treatment to the ramifications of the infected tissue. Aggressive surgical treatment of abdominal actinomycosis has been limited by the poor general condition of the patients. The role of supportive treatment (that is, high caloric intake, liberal transfusions) and of adjuvant chemotherapy is to restore and maintain the general condition of the patient at a

level tolerating repeated radical excision and curettage of the lesion. Favorable progress of the local lesion depends on meticulous wound hygiene, with the inhibition of secondary infection.

With the conscientious application of generous supportive treatment combined with radical surgical procedures the prognosis in extensive actinomycosis should continue to improve.

The Use of Absorbable Substances to Obliterate Bone Cavities and as Hemostatic Agents in Operative Procedures on Bones and Joints.—The use of oxidized gauze or absorbable gelatin with thrombin for hemostasis in the presence of troublesome oozing and bleeding has proved effective in difficult circumstances. The use of oxidized gauze is simpler than the use of absorbable gelatin and thrombin. The effectiveness of gelfoam has been found to be increased by investigators who have used suction to make it adhere to the bleeding area. The authors' [390] experience is limited to the simple application of the substance to the bleeding surface by pressure of the gloved finger or of an overlying piece of gauze, which is subsequently removed.

It is also apparent from the authors' limited experience that the use of these substances complicates the healing of the surgical wounds in an appreciable number of instances. These complications consist in the spontaneous evacuation of accumulations of blood and serum, with resultant temporary partial disruption of the wound. In at least one instance, ultimate failure of healing occurred as a result of secondary infection of such a temporarily disrupted wound. One should, therefore, weigh these possibilities carefully before resorting to the use of these hemostatic agents which in difficult circumstances are nevertheless of inestimable value in the control of oozing and bleeding.

The use of oxidized gauze or of absorbable gelatin as a vehicle for thrombin and penicillin in filling dead spaces or bone cavities appears to be inadvisable, from the authors' limited experience, because of the large proportion of complications interfering with the healing of the surgical wounds by first intention.

The use of oxidized gauze or of absorbable gelatin with thrombin as hemostatic agents in the presence of troublesome oozing and bleeding is advisable and at times invaluable, notwithstanding the fact that the final healing of the wound may, in a considerable proportion of instances, be delayed by temporary partial disruption incidental to the evacuation of collections of blood and serum.

Scheme of Treatment of Acute Hematogenous Osteomyelitis with Penicillin.—The following scheme of treatment has been drawn up at the Wingfield-Morris Orthopaedic Hospital as quoted from Trueta.

390. Buchman, J., and Blair, J. E.: The Use of Absorbable Substances to Obliterate Bone Cavities and as Hemostatic Agents in Operative Procedures on Bones and Joints, J. Bone & Joint Surg. **29**:650-658 (July) 1947.

Since June 1944, fifty cases of acute hematogenous osteomyelitis have been treated with penicillin at the Wingfield-Morris Orthopaedic Hospital, and there is now enough material to justify us in drawing up a routine plan of treatment which we are confident will, if followed in all its details, produce good results.

The following are the results to date:

No death
No amputation
No deformity
No joint infection after admission
No secondary focus after admission
No recurrence
No pathologic fracture or dislocation

Forty-nine of the 50 patients have full function. One patient, the second to be treated, has limitation of knee flexion (0—90 degrees). The abscess was not drained.

Forty-seven of the 50 patients (55 foci) have sound healing. Two patients, both with early, undrained femurs, have each a small sinus, and I adult has a small sinus from the ulna.

Sequestra have been obtained from 7 out of 55 infected bones.

(*a*) Three patients discharged a small sequestrum through the scar at home, without inflammation and with prompt rehealing (os calcis, metatarsal, fibula).

(*b*) In 1 case involving the humerus sequestrectomies have been performed; at the initial operation the upper third only was drilled: the early radiograph showed that the whole shaft had been involved.

(*c*) In 3 cases involving the femur sequestrectomies have been performed; the wounds had not been drained in spite of the presence of pus. (21 femurs were treated, of these 5 were improperly treated without surgical treatment.)

We think these results good enough to justify us in asking surgeons to adopt the method and principles described below for two reasons:

1. We are convinced that the method is an excellent one.

2. We should like to collect a series of 100 patients, with 100 per cent survival and function, treated in the Wingfield-Morris Hospital, by a method which, provided care is used, is simple enough to be carried out in all hospitals.

It is hoped, therefore, that treatment will be followed exactly, and sufficient records kept and investigations done, for an exact account to be given by whomever eventually writes up the series. The follow-up for several years at six or twelve monthly periods is especially valuable, and no patient should ever be discharged!

Principles of the Treatment

1. Acute hematogenous osteomyelitis is in part a systemic disease; therefore penicillin must be given systemically.

2. Systemic penicillin can resolve inflammation which has not advanced to pus formation: therefore surgical interference is not necessary in a case coming to treatment without evidence of pus formation (i. e., with only a small area of tenderness).

3. Systemic penicillin cannot sterilize preformed pus: therefore pus present before treatment must be removed surgically.

4. Systemic penicillin prevents the formation of fresh pus after removal of that already present at the onset of treatment: therefore complete primary suture is safe and is especially recommended because of the susceptibility of penicillin wounds to gram-negative infections.

5. The damage to the bone circulation in acute hematogenous osteomyelitis is due not only to the infection but to the increased tension within the bone impairing the blood supply; this tension is not relieved when the subperiosteal pus is evacuated. The bone should, therefore, be drilled in several places to allow the release of tension. Extensive bone work is not necessary.

6. The success and safety of this treatment depends on two important factors:

(*a*) The organism must be sensitive to penicillin. The initial dose used here allows for a staphylococcus of four times the normal sensitivity, but every effort must be made in every case to obtain a report of the organism and its sensitivity.

(*b*) The patient must get his penicillin. If a drip does not run for any reason the interval must be filled by regular intermittent injections. There is no excuse for a patient not getting his penicillin.

7. General medical measures, e. g., hydration of the patient, blood transfusion if necessary, immobilization of the part, and vitamin and iron therapy, are as necessary now as ever. Perhaps the most important measure is adequate hydration by mouth, by means of the penicillin drip, and if necessary intravenously. Most of these patients are dehydrated on admission.

Standard Courses of Penicillin Treatment in Acute Osteomyelitis

The doses are regardless of age and size and preferably given by intramuscular drip.

1. Days 1, 2 and 3.....400,000 units daily for the first three days, or, in a doubtful case, until sensitivity of the organism is known
   Day 4.....300,000 units
   Days 5 to 10+.....200,000 units daily, for a minimum of ten days, or until the sutures are removed, whichever is the longer.
2. .....400,000 units to cover any 24 hour operative period.

If intermittent injection is used, 100,000 units must be given every three hours to obtain a constant bacteriostatic level in the blood.

Practical Application of the Treatment

1. Patients in whom there is no clinical evidence of pus are treated with penicillin and with general medical measures. The area is immobilized in such a way that the local condition can be carefully watched. These patients usually have quick relief from pain and, compared with patients operated on, a rather slow fall in temperature.

2. Patients in whom there is probably pus present are treated with penicillin for twelve hours, and during that time immobilization of the part and general medical measures, notably hydration, are instituted. Patients must not go to the operating theater in a dehydrated condition.

3. Operation. This aims at: (1) removing as much pus as possible, (2) allowing the periosteum to renew its contact with the bone, (3) releasing the tension within the bone and (4) avoiding secondary infection by primary suture.

(*a*) A tourniquet is used wherever possible to ensure a dry field.

(*b*) The joint is aspirated, if there is fluid present, before operating.

(*c*) The incision is centered on the point of maximum tenderness; it is long enough for good exposure of the bone.

(*d*) As much pus as possible is removed from the tissue spaces surrounding the bone.

(*e*) The bone is drilled in at least two places. When pus is found, further drill holes are made up and down the bone until the limit of the pus is found or until the epiphysis or joint capsule is approached.

(*f*) The wound is sutured with interrupted sutures, without any form of drainage. Deep sutures are not used, but if a particular anatomic structure demands their use, surgical gut and not silk should be used.

(*g*) The part is elevated and immobilized in such a way that the wound can be easily inspected and gently palpated. Complete plasters or plasters with windows are always a nuisance, for it is good to look at both sides of the limb; the related joint should never be hidden.

We have found the following immobilizations the most satisfactory.

1. Lower half of femur, leg and foot—plaster back slab. Lower half of humerus, arm and hand—plaster back slab.

2. Upper half of femur and pelvis—hip frame.

3. Upper half of humerus—(*a*) arm in sling and bandaged to side for first three days, (*b*) thoracobrachial cast applied on the third or fourth day; the arm part is bivalved and only the lower half, supported if necessary by a strut, kept.

4. Postoperative and convalescent. Patients operated on are usually inspected about the fifth day for hematoma formation or minor infection of the sutures. The sutures are removed on the tenth day. The penicillin should be continued until the stitches are out. In all cases the bone is immobilized until the general and local conditions are beyond suspicion and until the bone is strong enough to avoid any risk of fracture. Solid sclerotic bone does not develop in these cases. The patient is discharged to his home for a month in plaster to allow for the increased activity.

The following details are important in the subsequent analysis of cases, and we should be grateful if they could be recorded in all cases.

1. *History*

Duration of symptoms, local and general
Stage at which general practitioner called, his diagnosis and treatment
Causes of delay in patient coming to treatment
Past history, trauma, recent infection, e.g., boils and chronic ear discharge

2. *Clinical Examination*

General condition
T. P. R., toxicity
Please record previous temperatures if known
Throat, ears, chest and renal tenderness
Palpation of entire skeleton for other foci
Local condition

Position of limbs, swelling, redness, tenderness, exact location of point of exquisite tenderness, which are diagnostic of the disease, fluctuation

Condition of related joints, lymphatic involvement

3. *Special Investigations*

X-ray of lesion and of chest.

Blood examinations: Complete count
Culture (taken before treatment begun)
E.S.R.
Blood group
Penicillin concentration if already treated

Urine routine ward and to laboratory for deposit.

Swab from any discharging lesions or suspect throat for culture and sensitivity.

4. *Provisional Diagnosis and Plan of Treatment*

5. *Operation Note in Detail*

6. *Postoperative Course. Penicillin Details*

7. *Duration of Healing. Duration of Hospitalization and Immobilization*

8. *Final Statement of General Condition, Healing Joint Condition, Lengthening or Shortening of the Affected Bone or Limb*

Note on Pathologic and Bacteriologic Specimens

Specimens for bacteriologic examination must be accompanied by a form on which it is stated clearly whether a sulfonamide or penicillin is being used so that the action of these substances can be inhibited.

The sensitivity of the organism to penicillin will not be tested unless it is asked for.

Blood culture syringes are specially sterilized and kept in the drawer in the Pathological Laboratory under the microscope. Please sterilize the skin carefully before taking a specimen.

Nonoperative Treatment of Acute Hematogenous Osteomyelitis: Preliminary Report.—That "acute hematogenous osteomyelitis is best treated with penicillin and that surgical intervention is rarely indicated" is concluded from results in a series of 14 cases.[391] Three case reports are presented in detail.

In all cases diagnosis was based on the history and the physical and laboratory examinations and was later confirmed by roentgenologic findings. Duration of symptoms ranged from one to thirty-five days, with an average of 7.9 days.

Penicillin was administered intramuscularly in all cases in doses of 10,000 to 25,000 units every three hours. Total dosage ranged from 960,000 to 6,040,000 units. In 6 cases sulfadiazine was given in addition for two to six days. The authors state that no increased benefit was observed in these cases.

391. Killeffer, J. J., and Robertson, R. C.: Non-Operative Treatment of Acute Hematogenous Osteomyelitis: Preliminary Report, J. Tennessee M. A. **40**:319-325 (Oct.) 1947.

The temperature became normal in two to eleven days, average 4.1 days, after the use of penicillin was begun. Treatment was continued for two weeks to two months after the temperature became normal.

There were no deaths in the series. Surgical treatment was required only once—incision of an abscess which had formed prior to admission. In 3 cases there was roentgenographic evidence of sequestrums which appeared to be revascularized. In 3 cases there was pathologic fracture resulting from inadequate fixation.

Infections of the Hands.—The value of penicillin in pulp space infection was studied in 100 consecutive cases in the outpatient hand clinic of a general hospital.[392] Personnel and methods of treatment were standardized. Cases included 69 of early simple felon, 20 of suspected bony felon and 11 of established bony felon.

Of the 100 cases of all types of felon, a pure culture of Staphylococcus aureus, penicillin sensitive, was grown in 99. In the remaining case, in which the finger was previously incised, Streptococcus hemolyticus was grown in the culture.

Principles of surgical treatment for simple felons and suspected bony felons included the lateral "hockey-stick" incision, division of the longitudinal septums and drainage of soft parts. Soaks, moist dressings and antiseptic baths were avoided. Instead, paraffin gauze dressings were used over a light film of penicillin powder.

Alternate patients among the 69 with simple felons were treated in addition with two intramuscular injections of penicillin, 100,000 units each, daily, for three days. No significant difference in morbidity time or in complications was observed in these patients.

In the 20 cases of suspected bony felon intramuscular injection of 100,000 units of penicillin twice daily for ten to twenty-one days proved adequate. Destructive osteitis was eliminated and the bone usually recalcified in a few weeks, without demonstrable sequestrums.

In 3 cases of established bony felon treated prior to this series by removal of the pulp and necrotic bone, results were disastrous. In the present series the surgical treatment was the same as that described for other types of felon. Penicillin, 100,000 units twice daily, was administered intramuscularly for at least two weeks. Every finger treated in this manner healed in eight weeks.

Penicillin in the Treatment of Acute Osteomyelitis.—There is yet to appear on the scientific horizon of therapeutic discovery an antibiotic that will match penicillin in its bacteriostatic power, its low tissue cell toxicity and the dramatic clinical response to it of patients infected with

392. Bolton, H.; Catchpole, B. N., and Japson, R. P.: Penicillin in Pulp-Space Infections of the Finger, Lancet **2**:608-610 (Oct. 25) 1947.

susceptible micro-organisms.[393] One has only to recall the ravages to the human body and the high death rate from sepsis wrought by the ubiquitous Staphylococcus aureus to appreciate the value of this marvelous drug.

It would appear that the hand of Providence has had a part in the discovery and development of penicillin, especially when one correlates its advent with the outbreak of the present global war.

Unfortunately, in treating osteomyelitis with penicillin, one may find an occasional infection with a penicillin-resistant staphylococcus.

It should be remembered that in a patient with a pocket of pus infected with a susceptible pathogen, even though the action of penicillin is not inhibited by organic matter such as pus (as are the sulfonamide drugs), it may not, for physical reasons, arrest the growth of staphylococci in the abscess and thus clinical symptoms may persist. It is recommended that drainage of such accumulations of pus be made, especially if clinical response be not immediately forthcoming. Again it is suggested that in cases not responding to penicillin one of the sulfonamides be prescribed and vice versa. There may also arise the occasional case in which both drugs may be used simultaneously to greater advantage.

It is reasonable to presume that the earlier therapy is instituted after the onset of symptoms in acute osteomyelitis the quicker will be the clinical response and the better the end result. Important, also, in this connection is the strong probability that the total required amount of penicillin necessary for complete sterilization of the focus will be much less.

Experience in treating a large series of cases, plus blood titration tests to establish minimal blood concentration of penicillin that will completely inhibit the growth of the offending micro-organism, will perhaps help to establish the necessary total dosage for each patient. Other pertinent factors to be considered, some being hard to evaluate in determining the total curative dosage of penicillin in each individual case, are the age of the patient, his resistance and the virulence of the micro-organism.

It was the opinion of Hamilton and Boyd at the time of writing that a safe method of procedure is to continue the use of penicillin for approximately five days after the temperature has returned to normal and that the total amount of penicillin used should be at least 1,000,000 units for patients with acute osteomyelitis.

The early and precipitous decline by lysis of the fever, along with obvious improvement in the well-being of the patient, is a favorable omen.

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393. Hamilton, J. F., and Boyd, H. B.: Penicillin in the Treatment of Acute Osteomyelitis, with Case Reports, South. M. J. **39**:597-608 (Aug.) 1946.

The economic factor in reducing the length of hospital residence as a result of penicillin therapy is astounding when compared with the use of any and all former methods of treating acute osteomyelitis.

Although the authors are aware that the number of patients they have treated is too small for factual conclusions, they prophesy that now since the supply of penicillin has become unlimited and the medical profession at large has become cognizant of its value and methods of application, "chronic osteomyelitis" will be almost a thing of the past.

They conclude that (1) penicillin is a marvelous and powerful antibacterial agent, (2) its discovery by Alexander Fleming was more or less an accident, (3) it acts as both a bacteriostatic and a bactericidal agent under certain conditions, (4) its high antibacterial power is coupled with low tissue cell toxicity and (5) it is reasonable to presume that since penicillin has become unlimited and the general medical profession is aware of its value "chronic osteomyelitis" will become almost a disease of the past.

Treatment of acute hematogenous osteomyelitis with penicillin prevents formation or causes dissolution of metastatic foci and disappearance of the primary osseous lesion within three to four weeks in approximately 90 per cent of the cases.[394] To obtain such results the treatment must be instituted early, the dose must be adequate, the medication must be continued for a sufficiently long period and the periosteal and metastatic abscesses must be drained.

The following steps are recommended by the author: (1) immobilization of the affected extremity in a splint for thirty to fifty days; (2) general treatment consisting of daily intravenous administrations of 1,000 to 2,000 cc. of dextrose or sodium chloride solution to combat dehydration, toxemia and acidosis, daily transfusions of 200 to 500 cc. of blood to fight bacteremia and secondary anemia, high carbohydrate diet and administration of vitamins; (3) administration of 15,000 units of penicillin intramuscularly every three hours, the total dose ranging from 1,000,000 to 5,880,000 units, according to the patient's resistance, the virulence of the micro-organisms and the time the treatment was initiated. The administration of penicillin is stopped two weeks after the return of the temperature and the leukocyte count to normal levels. Abscesses in soft parts are aspirated every third day, and 5,000 units of penicillin are injected. Administration of penicillin is supplemented by 20 to 30 Gm. of a sulfonamide compound.

394. Pires de Camargo, F., and Toledo de Carvalho, E.: A penicilina no tratamento da osteomielite aguda (consideroções sôlve 30 casos), Rev. Hosp. clín. **2**:1-8 (Jan.) 1947.

When such rules are observed, general and local clinical symptoms disappear rapidly, contrary to roentgenologic signs, which persist for a long time. This is due to the fact that penicillin transforms a septic necrosis into an aseptic one. The sequestrum acts like an autogenous graft which requires a certain time for its rehabilitation.

The authors report 30 cases of acute osteomyelitis in which early institution of treatment with penicillin and administration of sufficient doses prevented the development of a chronic form and avoided the necessity of an operation.

Surgical Problems in Patients with Diabetes Mellitus.—A brief review on surgical problems in patients with diabetes is presented, in which the author states that the use of penicillin has completely changed the concept of the management of carbuncles and has completely altered the approach to certain problems of the lower extremities in diabetic patients.[395]

The author states that formerly large carbuncles were a threat to the life of the patient. Treatment required wide excision and prolonged hospitalization. Now, with pencillin given intramuscularly in doses of 60,000 units every three hours, the lesion usually disappears in three to five days or becomes reduced to a small fluctuant area requiring a small incision. The author states that while carbuncles may be treated on an outpatient basis by penicillin in peanut oil or injected locally, hospitalization with intramuscular injections of penicillin is the preferred procedure.

Lesions of the lower extremities usually fall into three groups: (1) lesions which are primarily infections of a foot with adequate circulation, (2) lesions which are primarily due to defective arterial supply and (3) neuropathic ulcerations.

The use of penicillin to control infection makes possible procedures which were formerly too dangerous. Penicillin is administered in doses of 300,000 to 500,000 units daily (60,000 units every three hours) for at least twenty-four hours before operation and for five to seven days after operation. Operation above the area of gangrene and gross infection usually gives good results even when circulation is impaired. The author states that 92 transmetatarsal amputations were done, with no deaths and with satisfactory functional and anatomic results. It is stated that in cases in which one or more digits are involved, transmetatarsal amputation offers excellent insurance against later complications.

Antibiotics in the Surgery of Trauma.—A brief summary of the usefulness of the antibiotics (penicillin, streptomycin, tyrothricin and

395. McKittrick, L. S.: Surgical Problems in Patients with Diabetes Mellitus, Chicago M. Soc. Bull. **50**:235-239 (Sept. 27) 1947.

bacitracin) in traumatic surgery is presented, based on reports from the literature and the experience at the Henry Ford Hospital.[396]

The author states that the antibiotics have not obviated the need for orthodox surgery in the prophylaxis and treatment of infected wounds, but are valuable adjuncts. Ideally, their use should be accompanied with bacteriologic diagnosis.

The most widely used antibiotics are penicillin and streptomycin. The discussion of their usefulness has been presented under the following headings: injuries of soft parts; compound fractures; burns.

The author states that at the Henry Ford Hospital, treatment of lacerations in the emergency room consists of the usual surgical procedures without antibiotics. Patients with complicated wounds receive penicillin intramuscularly in doses of 12,500 units every three hours for five days. In cases of contaminated serous cavities penicillin is administered systemically and is instilled locally (100,000 units).

Penicillin may be administered by intermittent intramuscular injection, a daily injection of a beeswax-oil preparation or orally. In the author's opinion intermittent intramuscular injection is the most reliable.

In cases with gram-negative organisms resistant to penicillin but sensitive to streptomycin the latter drug may be administered intramuscularly in doses of 1 to 4 Gm. daily.

Penicillin has not been effective in tetanus although the tetanus bacillus is inhibited in vitro, but it is a valuable adjunct in the treatment of gas gangrene.

All patients with compound fractures at the Henry Ford Hospital receive prophylactic intramuscular injections of penicillin for at least two weeks—50,000 units every three hours for the first week and half this dosage for the second.

Penicillin is useful during the acute phase of a burn if symptoms of infection are present; it is especially valuable during skin grafting. Two illustrative cases of the latter are given. The first patient received 5,000,000 units intramuscularly and 1,500,000 units locally. Attempts at grafting were unsuccessful until penicillin therapy was instituted. The patient in case 2 received 12,500,000 units intramuscularly. The author states that streptomycin should be useful in burns with pyocyaneus infection.

Tyrothricin is effective against gram-positive cocci, but is suitable for topical application only. Bacitracin has been reported effective in a series of surgical infections due to cocci resistant to penicillin.

Use of Penicillin in Acute Infections of the Hand.—An evaluation of penicillin therapy in acute infections of the hand was carried out

396. Lam, C. R.: Antibiotics in the Surgery of Trauma, Am. J. Surg. **74**: 302-306 (Sept.) 1947.

in 260 unselected patients treated according to four different methods in the outpatient department of the Dundee Royal Infirmary.[397] Results were compared with those in 200 cases of acute infections of the hand previously treated.

All patients were treated by incision adequate for free escape of pus and removal of all sloughs. Drainage was maintained for forty-eight hours by packing with gauze impregnated with penicillin cream (100 units per gram). In group 4 paraffin gauze was substituted.

The length of disability in acute infection of the hand was not appreciably shortened by penicillin therapy. The author states that this is because infections are already localized and pus is present before the patient sees a physician.

In 7 cases seen early enough to attempt to abort the infection with parenteral administration of penicillin, the attempt was successful in only 3 instances. The author states that the best treatment for threatening pulp infections is early lateral incision.

The use of penicillin oil and wax resulted in general or local reactions in 8 of 87 cases.

No benefit was observed from the parenteral use of penicillin postoperatively.

Suppurative Arthritis of Hip Joint Treated with Penicillin.—Good final results were obtained with combined local and systemic penicillin therapy in 4 cases of acute suppurative staphylococcic arthritis of the hip joint reported from Suva, Fiji.[398]

Patients ranged in age from 6 to 16 years. All cases were presumably secondary to septic cutaneous lesions. In all cases aspirated pus yielded Staph. aureus.

Treatment in all instances consisted of intra-articular instillation of penicillin after aspiration (9,000 to 30,000 units) on alternate days for two to four injections, systemic administration of penicillin (20,000 to 30,000 units every three hours) for seven days and extension on Thomas' splint for ten days to four weeks. In 2 cases a hip spica plaster was applied after removal of the splint.

In all cases full movements of the joint were attained. Return of full movement was attained earlier in cases without plaster, suggesting its use to be unnecessary.

From results in these cases, the following regimen of treatment is suggested: immediate exploratory aspiration of pus, with replacement by an equal volume of penicillin solution (3,000 units/cc.) on alternate days until there is "local freedom from pain and examination of pus

397. Webster, A. L.: Use of Penicillin in Acute Infections of the Hand, Lancet **2**:610-612 (Oct. 25) 1947.

398. Gilchrist, K. J.: Suppurative Arthritis of Hip-Joint Treated with Penicillin: Report of Four Cases, Brit. M. J. **2**:450-451 (Sept. 20) 1947

shows absence or degenerate forms only of staphylococci"; intramuscular injection of penicillin (30,000 units/cc.) every three hours for a week; immediate immobilization, with extension, maintained until the patient is asymptomatic and afebrile; bed rest for four weeks, after which active movements of the joint are to be encouraged.

Chronic Osteomyelitis in War Wounded: A Report of Two Veterans Discharged With Intractable Osteomyelitis and Successfully Treated with Local Penicillin Detergent Therapy.—From the experience in the 2 cases reported [399] and with 37 civilian patients with chronic osteomyelitis, the authors conclude that "the mutilating treatment of osteomyelitis by radical surgery and cauterization is outmoded and should be replaced by conservative procedures employing antibiotics, as in the method described."

The method described employs a solution of penicillin in "aerosol O.T." 0.1 per cent (1,000,000 units in 50 cc.). This solution is instilled into the medullary canal by means of a T tube or a rubber catheter; 2 to 3 cc. is injected every three hours for ten days. An opening for the tube is made by excising the sinus tract down to the diseased bone and then curetting or drilling a hole.

The authors state that with the use of a detergent with penicillin there is a synergistic action on the efficiency of the latter.

Acute Suppurative Tenosynovitis Treated with Systemic Administration of Penicillin.—The effectiveness of intramuscular injection of penicillin in the treatment of acute suppurative tenosynovitis was investigated in 13 cases during 1946, and the results were compared with those in 13 unselected patients treated without penicillin in 1943.[400]

In 10 of the 13 patients selected for treatment the condition was frankly purulent at operation. Three of the infections were primary tendon sheath infections (infecting organism, Streptococcus pyogenes), 8 were finger pulp infections and 2 were superficial abscesses. The predominant organism in the secondary cases was Staph. aureus alone or in mixed culture.

Penicillin was started immediately after operation—12,500 units every three hours until a total of 1,000,000 units was given in ten days. The other principles of treatment were minimal incision and early active movements.

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399. Grace, E. J., and Bryson, V.: Osteomyelitis in War Wounded: A Report of Two Veterans Discharged with Intractable Osteomyelitis and Successfully Treated with Local Penicillin-Detergent Therapy, New York State J. Med. **47**:2204-2205 (Oct. 15) 1947.

400. Cruickshank, C. N., and Harrison, S. H.: Acute Suppurative Tenosynovitis Treated with Systemic Penicillin, Lancet **2**:606-608 (Oct. 25) 1947.

Eight of the penicillin-treated patients attained full function, and only 1 required amputation, while of the patients treated without penicillin, none attained full function and 9 required amputation.

For the penicillin-treated patients the medium healing time was twenty-seven days (maximum thirty-eight, minimum twelve). Medium healing time in the patients treated without penicillin was sixty-one days (maximum one hundred and eighty, minimum seventeen).

It is concluded that the effectiveness of intramuscular injection of penicillin has been established by these results.

Penicillin and the Treatment of Infected Hands in Outpatients.—The efficacy of the outpatient treatment of infections of the hand by intramuscular injection, twice daily, of large doses of penicillin in aqueous solution of beeswax oil was investigated.[401] Seventeen patients were so treated. Results were compared with those in 168 patients treated without penicillin.

Penicillin dosage was 300,000 units in aqueous solution or 100,000 to 150,000 units in beeswax oil twice daily. The condition of patients selected for penicillin treatment was clinically more serious than that of those treated without penicillin.

The average loss of duty for the 168 patients treated without penicillin was 20.3 days; for the 17 patients treated with penicillin it was 10.9 days.

Grouped according to diagnosis, the average loss of duty was as follows: paronychia and pulp space infection—without penicillin, 21 days, with penicillin, 9.9 days; tenosynovitis—without penicillin, 17.5 days, with penicillin, 9.9 days; palmar space infections—without penicillin, 16.5 days, with penicillin, 17 days (including a patient who became reinfected, prolonging loss of duty to 41 days).

Blood level studies demonstrated that administration of 150,000 units of penicillin in beeswax oil twice daily would provide continuous blood levels averaging 0.08 units per cubic centimeter; however, the peak level with this dosage is only 0.32 units. Clinically, both this dosage and 300,000 units in aqueous solution twice daily were considered adequate.

From these results it is recommended that penicillin therapy be routine in all severe infections of the hand, both in the early stages and after necessary surgical treatment.

Chronic Osteomyelitis as the Sequel to a Gunshot Wound.—According to an article by Perkins,[402] "operation rarely does any good" and

401. D'Abreu, F.; Flood, C. M., and Hewitt, H. B.: Penicillin and the Treatment of Infected Hands in Out-Patients, Brit. M. J. **2**:603-605 (Oct. 18) 1947.

402. Perkins, G.: Chronic Osteomyelitis, Sequel to Gunshot Wound, Brit. J. Surg. **34**:31-34 (July) 1946.

"excluding an operation on the bone, there are two courses open to the patient; one, to accept his lot and to be resigned to periodic flares which will keep him from work for several weeks once or twice a year; and the other, to lose his limb. Many a pensioner of the last war is today thankful that he was at last persuaded to have his leg amputated." The author also says "penicillin has not in my experience been of any benefit."

Outline of the Treatment of Acute Hematogenous Osteomyelitis.—With the advent of the sulfonamide drugs and penicillin, ideas on this subject have changed considerably.[403] It has been a change toward conservatism and away from the old tenets which demanded that an incision be made and bone chiseled away or drilled as soon as the diagnosis was made. The experience of Robertson, Hoyt and others with mounting numbers of cases emphasizes the wisdom of approaching the problem primarily from a nonoperative standpoint and reserving surgical intervention for those cases in which, in spite of adequate measures, pus fails to resorb and increasing tension and pain demand its release. Even in these circumstances surgical intervention should be minimal and for the purpose of drainage only, with as little damage to bone tissue as possible. With early diagnosis and good medical management, such cases should be few and far between.

If at all possible, the patient should be hospitalized. A complete examination should include roentgenograms of the involved part and of the chest. Laboratory work should include a complete blood count and urinalysis. The hemoglobin content and the white blood cell count should be determined daily during the early stages of the disease. In the presence of a hemolytic organism the blood picture serves as a guide for the administration of blood. Small blood transfusions up to 250 cc. depending on the age of the patient will do much to improve his resistance.

Fluid balance should be maintained by the intravenous administration of isotonic sodium chloride solution or sodium chloride and dextrose as required. In the presence of anorexia and lowered protein intake, protein hydrolysates should be added. In addition an adequate vitamin intake should be assured. Ascorbic acid, 50 mg. three times a day, thiamine hydrochloride, 5 mg. three times a day, nicotinic acid, 25 mg. twice a day, and percomorph liver oil, 10 drops three times a day, are given. When the oral route cannot be used, parenteral administration is carried out.

The involved part should be immobilized in a plaster of paris cast or other splint. This will add much to the comfort of the patient and

403. Lewin, P., and Scheman, L.: Symposium on Clinical Advances in Surgery: Osteomyelitis, S. Clin. North America **27**:183-207 (Feb.) 1947.

insure rest of the part. The plaster should include at least the joints above and below the lesion to insure absolute immobility. It may be bivalved to permit observation of the part.

Chemotherapy: Of the sulfonamide derivatives, sulfadiazine is the most commonly used and the least toxic. Children will tolerate large doses. The daily dose may be calculated on the basis of 4 to 6 grains (0.26 to 0.4 Gm.) per pound of body weight. The initial dose for an adult is usually 2 Gm. followed by 1 Gm. every four hours day and night.

Blood levels should be checked frequently and an effort made to maintain a level of about 10 mg. per hundred cubic centimeters. When the drug cannot be taken orally the sodium salt of sulfadiazine may be used in initial doses of 4 to 6 Gm. intravenously and a level maintained by the administration of 1 Gm. every four to six hours. Adequate fluid intake must be maintained to avoid crystalluria, and the urine must be checked frequently for hematuria or crystalluria.

Penicillin has replaced the sulfonamide drugs to a large extent in the nonoperative treatment of osteomyelitis; however, they can be given concomitantly, and in fulminating cases it is advisable to do so. While the sulfonamide drugs are bacteriostatic in effect, penicillin is bactericidal in its action. Penicillin is administered in a dilution of 1,000 units per cubic centimeter. The average daily dose is about 120,000 units administered in equal doses every three hours day and night. It may be given intravenously, 10,000 units every two hours, or 15,000 units intramuscularly may be given every three hours. The frequent dosage is necessitated by the rapid elimination of the drug. More severe cases will require up to 400,000 units daily. Overdosage is a better rule than underdosage inasmuch as the latter may lead to a certain amount of resistance on the part of the organisms.

With the management as described, it will be noted that many lesions and even sequestrums will not go on to suppuration and that healing and resorption may occur without abscess formation.

In many instances abscesses which form will recede and absorb without drainage. It has been the practice of Lewin and Scheman to aspirate and irrigate until the return is clear when an abscess presents externally. Several grams of microcrystalline sulfadiazine or 5,000 or more units of penicillin is instilled through the same needle. Osteomyelitis caused by streptococci may never suppurate. That caused by staphylococci does so more consistently.

If for any reason the abscess does not recede and increasing tension and pain indicate more adequate drainage, a simple decortication is done with as little trauma as possible, a small square of bone being removed. No currettage or other manipulation is done. The periosteum should be cleanly incised and not stripped any further than is necessary to remove this section of bone. The wound is lightly packed with petrolatum gauze, and a plaster cast is applied.

When effusion into the adjacent joint occurs, the joint should be aspirated to determine whether a pyarthrosis exists. If such is the case the primary focus in the bone should be left alone and the joint drained surgically by adequate incision. The joint is lavaged with calcium penicillin solution containing 250 units per cubic centimeter. Petrolatum gauze is inserted loosely into the wound, down to but not through the capsule. The wound is dressed and encased in plaster.

The subsequent care should be along the lines outlined by Orr. No windows are necessary in the casts, and dressings should be done as infrequently as possible and always under strict asepsis. The wounds will take care of themselves.

Chemotherapy Before, During and After Surgery: No hard and fast rules can be laid down, but in general it has been found that the following plan of treatment is adequate. Penicillin is given in doses of 30,000 units every three hours for a period of five days preoperatively. On the patient's return from the operating room 50,000 units are administered intravenously in isotonic sodium chloride solution. This is followed by 30,000 units intramuscularly every three hours for a period of three to five days postoperatively, the temperature reaction and blood count being used as the guide.

Penicillin and sulfathiazole powder are used locally after débridement in the proportion of 10 Gm. of the sulfonamide drug to 150,000 units of penicilllin. When irrigation of the wound is deemed advisable postoperatively, it is done through a tube leading into the gauze pack. A solution of calcium penicillin in distilled water is used. In certain cases a penicillin-fast organism may be encountered which will respond readily to a sulfonamide drug. In such cases sulfadiazine may be used. Frequently it appears advisable to administer both drugs.

Streptomycin has not as yet been found to be beneficial in osteomyelitis.

It must also be remembered that an optimal time for surgical intervention must be sought. Toward this end, the general condition of the patient must be brought up to the best possible level. Blood transfusions should be given to bring the red blood cell count and the hemoglobin content up and to supply immune bodies by passive transfer. When the patient's nutrition is deficient, an adequate intake should be assured, by a parenteral route if necessary.

Protein hydrolysates are available for intravenous administration. An adequate vitamin intake is necessary for the patient's general well-being, for bone repair and for capillary formation. A high vitamin, high caloric diet is the rule when the patient can take it. The surgical treament of chronic osteomyelitis is not urgent, and the time spent in bringing the patient's condition up to an optimum level is time well spent.

PROGRESS IN ORTHOPEDIC SURGERY FOR 1946

A Review Prepared by an Editorial Board of the American Academy of Orthopaedic Surgeons

X. CONGENITAL DISLOCATION OF THE HIP

Prepared by

A. BRUCE GILL, M.D., PHILADELPHIA

TRASK [404] reports the case of a female child born at term by spontaneous delivery. Roentgenograms of the pelvis including the hip joints, made after delivery because of the presence of a small cutaneous depression at the level of the lumbosacral joint, revealed a slight outward and upward displacement of the right femur. The condition was apparently overlooked at the time of the examination, and no treatment was advised. One and a half years later the child had a complete dislocation of the right hip. There was no family history of congenital deformities. This case proves that congenital subluxation (or predislocation) of the hip may be present at birth and that the condition may be recognized by roentgenographic examination at this early date.

[ED. NOTE.—This type of dislocation probably occurs during late fetal life.]

Ensthaler [405] describes 2 cases of coxitis or osteomyelitis in newborn infants who had congenital dislocation of the hips. The congenital dislocation can be differentiated from pathologic dislocation only if the congenital deformity is recognized before the coxitis has developed.

The history of the treatment of congenital dislocation of the hip has been reviewed by Hass.[406]

Da Gama [407] states that it is possible to produce a fracture of the neck of the femur in the process of bloodless reduction even with the greatest care on the part of the surgeon and that spontaneous fractures may occur during the period of continuous extension. He reports a case. He ascribes this condition to pathologic changes in ligaments, muscles, nerves and bony structure that accompany congenital dysplasia of the hip.

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404. Trask, B. W.: Congenital Dislocation of Hip: Report of Case, Am. J. Roentgenol. **55**:331-332 (March) 1946.

405. Ensthaler, J.: Ueber zwei Fälle von angeborener Hüftverrenkung mit Säuglingskoxitis, Ztschr. f. Orthop. **75**:65, 1944.

406. Hass, J:. Congenital Dislocation of Hip: Fifty Year Survey, J. Internat. Coll. Surgeons **9**:152-158 (Jan.-Feb.) 1946.

407. da Gama, C.: Luxação congênita do quadril: Responsabilidade médica, Publ. méd., São Paulo (no. 8-9) **16**:11-27 (March-April) 1945.

[ED. NOTE.—I have encountered no case similar to this. But I have observed one in which there was a prolonged delay in calcification of the femoral neck. It is understandable that in such a case fracture of an uncalcified neck might readily occur.]

Von Haberier [408] expresses the belief that in many cases congenital dislocation is fully developed at the time of birth. He states that such conditions can be easily recognized at birth. He treats them by recumbency in a plaster mold or bed with the legs abducted. The child is fastened in this plaster bed with bandages and can be removed from it for bathing and change of diapers. In the past three years the author has observed 60 cases which were diagnosed during the first few days of life. In 33 of these the condition was bilateral; in 22 the left hip was involved and in 5 the right hip. There were completely developed luxations in 14 of the cases in which there was bilateral involvement and in 22 of the cases of unilateral involvement.

Von Haberier continues the treatment until the roentgenograms show a well developed acetabulum. The treatment may require from six weeks to eight months, with an average of three and a half months. He emphasizes the importance of early diagnosis and of treatment by abduction.

[ED. NOTE.—In this country we do not have adequate statistics on predislocations and complete dislocations that are recognized at birth and immediately treated. The opinion is generally accepted that early restoration of normal mechanics by complete conjugation of the acetabulum and the femoral head promotes and hastens complete cure. It has been observed, however, that in some cases predislocation is not cured within eight months after treatment is begun. This may be due to the fact that the condition has not been recognized and treated from birth, or it may be due to an innate inability of some hips to make a rapid or complete recovery even under favorable mechanical conditions.]

Compere and Schnute [409] believe that the most common cause of failure to secure perfect results from bloodless reduction of congenital dislocation of the hip is the discontinuation of fixation in abduction too soon after reduction. They express the opinion that if abduction is maintained for a sufficient length of time a normal acetabulum will develop in accordance with Wolff's law. They recognize the danger of atrophy that is inherent in prolonged fixation in plaster casts and advocate the use of spreader splints and modified Denis Browne splints

408. von Haberier, G.: Neue Erkenntnisse der angeborenen Hüftgelenksverrenkung und ihrer Behandlung, Ztschr. f. Orthop. **75**:38, 1944.

409. Compere, E. L., and Schnute, W. J.: Treatment of Congenital Dislocation of Hip, J. Bone & Joint Surg. **28**:555-564 (July) 1946.

to maintain the required degree of abduction while permitting voluntary motion of the hips in flextion and extension.

[ED. NOTE.—If a luxation can be reduced, the reduction can be maintained by abduction combined with internal rotation in cases of marked anteversion. Dysplasia of the acetabular roof may or may not become corrected by natural growth processes. The authors' case reports and illustrations are too few to enable the reader to draw any conclusion. Maintenance of reduction does not always lead to normal development of the acetabulum. Furthermore, there is no reason to believe that long-continued abduction will bring about correction of such deformities as shortening of the femoral neck, high attachment of the capsule and pronounced dysplasia of the femoral head.]

Tavernier [410] discusses the various methods of treatment of old irreducible congenital dislocations of the hip. He has abandoned the use of resection of the femoral head and arthrodesis of the hip. Reconstructive plastic surgery is indicated from puberty up to 25 or 30 years of age, but the operations are merely prophylactic and are not always successful. In bilateral dislocations Tavernier operates on the one hip. If the result is good he then operates on the other hip.

[ED. NOTE.—This principle is correct because one cannot risk making two stiff hips.] If a posterior dislocation is well tolerated, the patient is usually advised to postpone operation until the symptoms become aggravated. In bilateral high dislocation with annoying lordosis and adduction deformity, double osteotomy is indicated. However, the author states that if excessive rigidity is present arthroplasty may also be considered in place of osteotomy. Resection of the nerves to the hip joint is indicated when pain is the predominating symptom, either before or after other types of operation. A typical indication for nerve resection is the instance in which the patient has had good walking ability for years in spite of the dislocation and then after a varying length of time suffers disabling pain. The nerve resection frequently enables the patient to walk again as well as he did formerly. Previously the author resected only the articular fibers of the obturator nerve, but more recently he has included the articular fibers from the sciatic nerve, with better results. Of 19 cases of nerve resection, excellent results have been obtained in 9, fair results in 8 and no improvement in 2. The operation may not only relieve pain but may also improve motion by relieving the muscle spasm which is due to pain.

[ED. NOTE.—This operation apparently has a definite usefulness in particular cases. Reconstructive operations may succeed equally well in

410. Tavernier, L.: L'enervation articulaire dans le traitement des luxations congénitales de la hanche chez l'adulte, Lyon chir. **41**:45-50 (Jan.-Feb.) 1946; Rev.d'orthop. **32**:109-116 (May-Aug.) 1946.

relieving pain by increasing the stability of the hip and thus removing chronic strain.]

From a study of 750 cases of congenital dislocation of the hip Bargellini [411] concludes that treatment during the first year of life, when the condition is only predislocation or subluxation, yields vastly better results than treatment at a later period. In some cases observed five years after reduction the clinical results were perfect and the roentgenograms showed only the slightest suggestion of the primary coxofemoral dysplasia. In other cases there was already evidence of persistent dysplasia of the femoral head, called by the author Calvé-Legg-Perthes disease, which eventually recovered without clinical symptoms.

[Ed. Note.—Undoubtedly many of these hips were left with permanent deformity of the femoral head and corresponding deformity of the acetabulum which would produce symptoms in later years.]

Bargellini records excellent results after five years in 20 per cent of the cases, good results in 50 per cent and mediocre results in 30 per cent.

[Ed. Note.—This end result study cannot be considered to be complete because the cases were under observation for only five years. Clinical symptoms may arise in many cases in which at the end of five years the condition is considered good or satisfactory because the patient is free from symptoms. The author's 20 per cent excellent results corresponds with the percentage of perfect results (perfect function and perfect or almost perfect anatomy) recorded by me. But the 50 per cent good results, which presumably means freedom from symptoms, would undoubtedly be much reduced on reexamination in later years.]

Colonna [412] describes his method of arthroplasty for congenital dislocation of the hip in children. The first stage of the procedure consists in pulling the head of the femur down completely to the level of the acetabulum. Skeletal or skin traction may be necessary for a number of weeks to secure complete stretching and relaxation of the soft tissues. When this has been accomplished, operation is performed. Through an anterolateral incision the entire capsule of the hip joint is exposed and freed from surrounding muscles. A transverse incision is then made completely through the capsule at its narrowest point or isthmus. The head of the femur is inspected. The distal margin of the severed capsule is then sutured over the head of the femur, which thus is completely enclosed in a capsular sac. The primary acetabulum is then

411. Bargellini, D.: Considerazioni su settecentocinquanta lussazioni congenite dell'anca curate con il metodo di Paci Lorenz entro il primo anno di vita e riesaminate ad oltre cinque anni dalla riduzione, Arch. ortop. **56**:3-28 (July) 1940.

412. Colonna, P. C.: Arthroplasty for Congenital Dislocation of Hip, J. Internat. Coll. Surgeons **9**:51-55 (Jan.-Feb.) 1946.

enlarged, deepened and rounded sufficiently to receive the entire capsule-covered head. The head is placed in the new acetabulum, the wound is closed and the lower extremity and the trunk are fixed by a plaster cast to maintain full extension and slight abduction of the hip. The cast is removed at the end of four weeks. Five to 10 pounds (2 to 45 Kg.) of traction is employed during the next few weeks. Active and passive movements are given after removal of the cast. Abduction and flexion contractures must be prevented. Walking is begun in from three to six months after the operation.

Colonna considers this operative procedure to be indicated for (1) children under 3 years of age in whom reduction cannot be obtained by bloodless manipulation or in whom redislocation has occurred after a primary reduction and (2) children from 3 to 10 years of age in whom it is possible to pull the head of the femur down to the level of the primary acetabulum. The essential contraindication is an inability to obtain preliminary stretching of soft tissues sufficient to bring the head of the femur to the level of the acetabulum. This factor is dependent largely, but not entirely, on the advancing age of the child.

Colonna describes 5 patients who have been followed for from ten to thirteen years after operation. They have stable, well formed hip joints, excellent range of active and passive motion and no limp.

[Ed. Note.—As pointed out recently by Colonna, the best results followed the use of this procedure for unilateral dislocation in children under 8 years of age.]

Ponseti [413] analyzes results following the shelf operation in 70 cases of congenital dislocation of the hip from the service of Dr. Steindler, at Iowa State University. Seven other cases of dislocation due to infantile paralysis, spastic paralysis and suppurative arthritis are included in the report. The age of the patients at the time of operation varied from 2½ years to 36 years. In 42 cases the shelf was built over a femoral head which was placed in the primary acetabulum. In the others palliative operations were performed for irreducible dislocation. In 27 cases closed reduction had been done from one month to sixteen years before the shelf operation. In 50 cases the operation was performed with or without concomitant closed reduction.

Of 7 patients with prenatal dislocations operated on between 2½ and 5 years of age, not one had a good anatomic or functional result.

[Ed. Note.—If these hips fall in the group which present severe deformities at birth, one should not expect to obtain good results by

413. Ponseti, I.: Pathomechanics of Hip After Shelf Operation, J. Bone & Joint Surg. **28**:229-240 (April) 1946.

operation. They are irremediably dislocated, and only palliative operations are possible.]

Twenty-three patients under 6 years of age were operated on for postnatal dislocation of the hip. In 5 of these the femoral head was not placed in the primary acetabulum, and the results were anatomically and functionally poor.

[ED. NOTE.—These results should be expected, as the operations were only palliative.]

In 18 cases the head was in the primary acetabulum. The results were a "well developed hip" in only 1 case and a "moderate deformity of the hip" in only 3 cases. Five operations resulted in "dysplasia, not subluxation," two in subluxation and seven in "head in secondary acetabulum." The functional results were correspondingly poor. In only 4 patients was there an absence of symptoms.

[ED. NOTE.—One should obtain better results from well executed shelf or "buttress" operations in this type of dislocation. This subject is discussed in the following paragraphs.]

Thirty-one hips were operated on for postnatal dislocation. The patients were over 6 years of age. In 15 cases the shelf was formed over a head which lay in a secondary acetabulum and in 15 cases the head was in no acetabulum. The results in these 20 cases were anatomically and functionally poor. Of 9 cases in which the head was in the primary acetabulum, only 1 resulted in a moderate deformity of the hip, with freedom from symptoms, while the remaining 8 resulted in "dysplasia" or "head in secondary acetabulum," with the presence of symptoms.

Of forty-two hips operated on with the femoral head in the primary acetabulum, only six became satisfactory, one became fused after a forcible reduction and thirty-five became subluxated or dysplastic, with pain, limp, limitation of motion or all three of these symptoms. In the successful cases the head of the femur remained in the primary acetabulum; in the instances in which the operation failed it moved outward and upward. When the femoral head is situated too far from the central weight-bearing line of the body, a positive Trendelenburg sign and a limp must be present. Ponseti states that in most cases the shelf was built at the upper end of a sloping acetabular roof, and when the patient started to walk the femoral head slipped outward and upward until it came to rest beneath the newly constructed shelf.

[ED. NOTE.—I have repeatedly emphasized the importance of correcting the obliquity of the acetabular roof and of constructing the shelf as an integral part of this reflected roof so that the roof with its added extension covers snugly and accurately the entire upper portion of the head of the femur. If this operation is performed properly, the head of

the femur can never thereafter travel upward and outward. This paper demonstrates not the futility of the "shelf" operation per se but rather the poor results of inadequate surgical treatment. When the head of the femur does not lie in the primary acetabulum or cannot be placed within it by gentle manipulation, the shelf operation should be considered as a palliative procedure which cannot be expected to produce a perfect hip but which will relieve or abolish some of the symptoms, particularly pain and disability, if the operation is properly done. This paper on the end results of the shelf operation, like similar previous papers, serves chiefly to demonstrate the poor results that may be obtained by doing a good operation badly.]

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